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STUDIES ON THYROID DISORDERS: VII

# CORRECT AND INCORRECT USE OF IODINE IN THE TREATMENT OF GOITER

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MANY centuries ago it was established that the ashes of sponge and seaweed had a beneficial effect upon certain cases of goiter. It was naturally not known that this benefit was produced by the therapeutic action of the iodine contained in this ash. Finally toward the beginning of the nineteenth century it was recognized that iodine in pure form cured or greatly improved many patients with goiter. Coindet,[1] quoted by Plummer,[2] reported his successes in Switzerland in a publication on this subject in 1820. By virtue of a mistake in prescribing 15 to 20 drops of tincture of iodine per day for a fortnight to a patient very ill with exophthalmic goiter Trousseau[3] in 1863 produced a typical clinical remission in the severe clinical manifestations of the disease. The pulse, which was counted at the rate of 140 to 150, dropped to a rate of 90 at the end of the treatment with iodine. Trousseau was not deceived by this favorable result for he immediately warned that iodine generally does harm in Graves' disease. Since that time the literature pertaining to the treatment of goiter with iodine has grown to tremendous proportions. Space will permit reference to a few only of the important contributions on the relationship of iodine to goiter. Baumann[4] in 1896 was the first to demonstrate that the thyroid gland normally contains iodine. Later he and his co-workers (Oswald[5]) demonstrated that iodine administered to animals is stored in the thyroid gland; that when there is a deficiency or absence of iodine in the diet of animals a compensatory colloid hypertrophy of the thyroid gland occurs; that the content of iodine in the thyroid gland is directly proportional to the amount of colloid and that the percentage of iodine in colloid goiter is relatively far less than in the normal thyroid gland. The iodine of the thyroid gland is contained in the globulin which Oswald called thyreoglobulin and which contains the entire active principle of the gland. Kocher,[6] although realizing the benefits to be derived from the treatment of endemic goiter with iodine, as early as 1907 warned against its use in all goiters showing signs of activity for fear of producing more serious results. He stated emphatically that treatment with iodine ultimately is more dangerous than the operation of thyroid excision. This statement is just as true today.

In a series of publications between 1908 and 1911, Marine[7,8] in collaboration with Williams and with Lenhart showed that there is a very definite relationship between the iodine content and the histological structure of the thyroid gland. They found

that in all the animals studied by them, cellular hyperplasia and hypertrophy are due to a deficiency of iodine or conversely, that in general the iodine store in the thyroid gland varies directly with the amount of stainable colloid and inversely with the degree of active hyperplasia. They found furthermore that when iodine is given to an animal with a hyperplastic thyroid, the gland immediately returns to the colloid or resting state, the nearest approach to the normal that a gland which has once been hyperplastic can make. These experiments together with those of Baumann[4] in 1896 were the first to demonstrate that there is a definite relationship between the histological structure of the thyroid gland and the intake of iodine. In other words, when the iodine intake is insufficient, colloid hypertrophy results and a hyperplastic thyroid can be made to revert to the colloid state by the administration of iodine. Kendall[9] in 1914 isolated the crystalline, iodine-containing, active principle of the thyroid gland and called it thyroxin. This substance has been shown to have all the active physiological properties of desiccated thyroid gland. In 1917 the prophylactic use of iodine for the prevention of simple goiter in man was started through the public schools of Akron, Ohio, by Marine and Kimball.[10] Iodine was also advised in the treatment of simple colloid goiter especially in the young.

Loewy and Zondek,[11] in 1921, showed that the increased metabolic rate in exophthalmic goiter could be markedly reduced and in some cases even a normal rate could be obtained by the administration of potassium iodide. Furthermore there was a concomitant improvement in clinical symptoms together with a gain in body weight. This improvement was, however, only temporary. In 1923, Plummer drew attention to the beneficial effects of Lugol's solution when administered as a preliminary preoperative treatment in cases of Graves' disease or exophthalmic goiter. He showed, in a large series of patients with this disease, that the majority was greatly benefited, and that practically in no instance were the symptoms made worse. Following the treatment with iodine there was a remission in the manifestations of the disease, and during this remission operation was performed. There was an immediate drop in the number of postoperative crises, and the convalescence was made relatively very comfortable. Since the publication of these results the intensive preoperative preparation of the hyperthyroid patient with iodine has come into general practice.

Unfortunately a veritable wave of incorrect use of iodine has engulfed medical practice and has marred the good results obtained by the correct use of iodine in the treatment of simple colloid goiter and in the preparation of the hyperthyroid patient for operation. As with many potent agents which have a decidedly beneficial therapeutic value when correctly used but which when incorrectly used may produce serious and even dangerous results, so it is with iodine, the incorrect use of which is today causing untold damage and great suffering to unsuspecting goitrous patients throughout our country. The surgeon is in a favorable position to observe the ultimate results of the incorrect administration of iodine, for the patient with goiter, toxic or non-toxic, who receives iodine indiscriminately commonly develops symptoms of acute hyperthyroidism, leaves the physician and finally consults the surgeon with reference to operation. Thus the physician unfortunately fails to see the final result of his therapy, and the surgeon is often confronted with a serious problem, difficult to treat because of a variety of unfortunate and even dangerous therapeutic results to be subsequently described. The incorrect and indiscriminate use of iodine has become so wide spread not only because of the extensive prescription of the drug by physicians but because of frequent dispensing by druggists and upon advice of the laity when it is not actually self-administered. Thus iodine is

administered not only as a solution or tincture of the metallic iodine, but also in the form of iodides, ointments, salves, tablets and table salt. The drug produces its characteristic effect regardless of the form in which it is administered or the manner in which it is introduced into the body, whether per os, per rectum, through the skin or intravenously. Normally iodine is taken into the body in the food and drink and even to a small extent in the air we breathe.

There is but one type of goiter, considered etiologically, that has been shown to have a definite relationship with the intake and metabolism of iodine and that is the so-called simple colloid goiter of childhood or early adolescence. It has been definitely shown that this inactive type of goiter commonly develops whenever there is a deficiency in the intake of iodine or a faulty metabolism after it has been taken into the body. Consequently it is rational to increase the iodine intake in patients with simple colloid goiter. It seems to me that this is the only type of goiter in which the therapeutic administration of iodine is indicated. Consequently it becomes of the greatest importance to correctly diagnose the type of goiter in order to institute correct therapy and avoid serious mistakes. By far the great majority of goiters for which the physician is consulted will fall into three groups: (1) the simple colloid goiter of the adolescent period; (2) the adenomatous or nodular goiter, toxic or non-toxic, and (3) the diffuse hyperplastic thyroid of Graves' disease or exophthalmic goiter.

### SIMPLE COLLOID GOITER

This form of goiter occurs at the adolescent or pre-adolescent age but may also occur as the large colloid goiter of young adults. In the former the thyroid gland is diffusely, symmetrically enlarged. It has a soft, elastic consistency, the surface is relatively smooth, definite irregularities are not felt and there is no increased vascularity as is indicated by the absence of pulse, thrills and bruits at the poles of the gland. There are no symptoms of hyperthyroidism and the pulse is not accelerated. Much experimental work has been done by Marine and his co-workers in the prevention of this condition both in humans and in animals by the administration of small amounts of iodine. Since simple colloid goiter seems definitely to be due to a lack of iodine, this drug is administered in small quantities to children of school age. In speaking of prophylaxis or treatment with iodine it is well to emphasize that the dosage of actual iodine should be considered in terms of milligrams.

*Treatment.* In 1917 Marine and Kimball[10] demonstrated the efficacy of iodine in the prevention of goiter in the school children of Akron, Ohio. Two grams of sodium iodide were given over a period of two weeks each spring and fall. They further suggested that maximum results would be secured by the administration of 5–10 mg. of iodine per week throughout the school year and that the dangers of giving too much iodine during a short period would thus be avoided. Soon after this work appeared, Klinger[12] adopted a similar manner of treatment for the prevention of endemic goiter in Zürich, Switzerland. Similarly good results were obtained. Iodine is conveniently administered in the form of the chocolate tablet devised by Klinger[13] and called "iodostarine," each tablet containing 10 mg. of iodine in a stable organic iodide. The tablet has the advantage of being pleasant to take. One tablet is given once a week during the school year. Jackson[14] has reported some good results after following this method of treatment in a considerable number of cases of colloid goiter.

When a colloid goiter has once become evident, specific medication is indicated, particular caution being exercised against the administration of iodine in excessive amounts. Regardless of the compound of iodine prescribed, and it matters little in what form iodine gains entrance into the system, the dosage should not be more

than 10 mg. of actual iodine per day or every other day, in the case of children. In young adults the dosage may be safely increased to 15 mg., always under supervision to detect any symptoms of hyperthyroidism. The iodine may be administered in the form of the syrup of ferrous iodide, sodium iodide, or syrup of hydriodic acid. But here again the tablets of iodostarine are a convenient form. The treatment is often unsuccessful because both the physician and patient may expect too prompt improvement in a few months whereas the treatment, to be successful, must often be continued for a year or more. The factors producing the shrinkage of the gland are not clearly understood. We do know, however, that there is a diminution in the amount of colloid with a consequent decrease in the size of the gland. I have found it advantageous to administer small amounts of thyroid extract in addition to the iodine, a more rapid improvement being thus obtained. In young individuals ½ grain of the thyroid extract is given daily or every other day and in older individuals with large colloid goiters, a daily dose of 1 grain of thyroid extract is thus given. Here again supervision is necessary and the results may be controlled by frequent metabolic rate determinations. At the first signs of activity, indicated by nervousness and increase of pulse, the medication is diminished or temporarily stopped. The thyroid extract increases the circulation generally and also in the gland and may thus exert its favorable effect. It may be said that in individuals over twenty years of age, treatment is apt to be unsatisfactory if not wholly disappointing, and surgical partial excision is occasionally necessary to relieve an ugly cosmetic appearance or symptoms of pressure.

When iodine is indiscriminately administered to the simple colloid goiter over a considerable period, symptoms of thyroid activation may appear and finally unquestionable hyperplastic changes may occur in the gland. The inactive gland is converted into the active hyperplastic type bordering on Graves' disease if not actually of the exophthalmic type, with the consequent production of hyperthyroidism, which may yield only to surgical measures. Kocher long ago pointed this out when he warned against the too free use of iodine for fear of producing what he called iodin-Basedow.

### IODINE IN PREGNANCY

The indication for the administration of iodine in a case of goiter depends at all times, it seems, upon the functional state of the gland. Consequently the medication with iodine during pregnancy should be decided upon only when thyroid inactivity is present. The pregnant state is not the determining factor. The administration of iodine to pregnant mothers living in goitrous districts has been advised for the purpose of preventing cretinism or hypothyroidism in the offspring. If the mother has a definitely subfunctioning colloid goiter this treatment would seem rational. It so happens, however, that during pregnancy the thyroid gland commonly undergoes varying degrees of hyperplasia and hypertrophy and shows varying degrees of activity, as indicated by symptoms of hyperthyroidism and increased metabolic rate. Consequently the gland is more sensitive to iodine than at other times. Accordingly the administration of iodine, even in small amounts, is in my opinion contraindicated. I have seen acute hyperthyroidism produced by the administration of iodine in too large doses during pregnancy. Thus iodine should preferably not be given except in the case of a subfunctioning thyroid. An example is the case of a woman who was worried over a simple colloid goiter and who feared to become pregnant on account of it. Accordingly iodine was administered in appropriate dosage over a period of three months and was then discontinued with the result that the goiter became definitely smaller. Some months later she became pregnant and as a prophylactic measure

against the return of the colloid enlargement, she was again treated with iodine in the former dosage. There was a prompt appearance of hyperthyroidism, necessitating the discontinuance of iodine, whereupon there was a rapid subsidence of the symptoms. The use of iodine during pregnancy is advocated for women living in goitrous districts, provided they have not developed adenoma of the thyroid gland and for those having a definite simple colloid goiter. One tablet of iodostarine (10 mg. of iodine) three times per week for pregnant and lactating women is recommended.

### NON-TOXIC ADENOMA

The true adenoma of the thyroid is an encapsulated rounded tumor of thyroid tissue. It may be single or multiple, causing the goiter thereby formed to be asymmetrical and nodular. Any thyroid swelling which is definitely nodular is presumed to be adenomatous. The circulation in such a goiter is rarely excessive as indicated by the usual absence of thrills and bruits in the thyroid arteries. The adenoma may contain any type of thyroid parenchyma resembling the so-called "fetal" structure, the colloid appearance or the hyperplastic glandular tissue characteristic of Graves' disease. As a consequence the nodule may be unassociated with symptoms of hyperthyroidism or it may cause symptoms characteristic of mild or severe hyperthyroidism. When unassociated with symptoms, particularly in the early stages of development, the adenoma is considered quiescent. There is no convincing evidence that the administration of iodine ever has a beneficial effect upon a true adenoma in the sense of causing its disappearance or halting its advance, even after prolonged use of the drug. Since this is the case, why should one ever administer the drug for the medical treatment of true adenomata? It seems to me from the reports in the literature and from my own experience that iodine, even in minute amounts administered over a period of several weeks or months, commonly activates a non-toxic adenoma, and often causes an exacerbation of symptoms in the toxic adenoma. Since the non-toxic adenoma is very prone to become toxic, particularly in later years, and because of the possibility of malignant degeneration in 6–10 per cent of the cases, operative removal, which carries practically no risk whatever, is the treatment of choice. Iodine for therapy is contraindicated and as a preoperative preparation is unnecessary.

### TOXIC ADENOMA

When an adenoma becomes activated, it secretes a toxic active principle similar to or akin to that secreted by the exophthalmic goiter. This toxin produces a pure hyperthyroidism such as can be produced by thyroxin or thyroid extract. The status of the patient rapidly returns to her previous normal when the source of the toxicity, the adenoma, is removed. During the early months or years in the life of a toxic adenoma, the symptoms are commonly insidious and undermine the health long before the patient is aware of the nature of her chronic illness. She may endure her symptoms many years before she consults a physician. Later, during a period of acute toxicity, the syndrome of acute hyperthyroidism is clearly evident. By this time serious damage has often been done to the general health, and particularly to the cardiovascular and nervous systems.

Iodine should not be given with the idea of a beneficial therapeutic effect upon active adenomata, of any degree of toxicity, and its use in such instances is most heartily to be condemned. The surgeon commonly sees patients with toxic adenoma in whom there has been a definite exacerbation of symptoms produced by iodine. Mild symptoms are converted into severe ones and acute hyperthyroidism is often converted into crisis with occasional death. I have had this lesson impressed by patients consulting me with reference to the operative treatment of

acute hyperthyroidism. It is interesting, furthermore, that such exacerbation is particularly prone to occur after administration of small amounts of iodine, over a considerable period of time rather than after large amounts administered over shorter periods. It seems best when one is confronted with such an exacerbation to continue the iodine for, when this is discontinued for three to six weeks, the exacerbation of symptoms may become even more severe. If iodine treatment is interrupted with the hope of causing a subsidence of symptoms, a return to the pre-iodine status may occur after the lapse of several months. In a case of toxic adenoma, activated by iodine, the further treatment with iodine even in large doses produces unfortunately little or no improvement, or the condition may be made progressively worse. This situation is one of the most serious problems the surgeon is called upon to face. Stage operations such as ligations, are of little value, as the thyroid arteries are relatively small, and not comparable to those seen in exophthalmic goiter. Accordingly scant reduction of circulation is obtained by ligation. The critical nature of such a case may not be comprehended by the surgeon, the basal metabolic rate may be only moderately elevated, and its value as a criterion of operability is obscured by the iodine medication. Operation may be undertaken with disastrous result. The risk of operation is unquestionably increased in instances where there has been previous indiscriminate treatment with iodine. In such cases of iodine exacerbation, it may be safer to allow the patient one or two months of sedative treatment with discontinuance of iodine, to be followed by intensive preoperative treatment with iodine. The mortality statistics under such precautions will be better.

The next question arises as to the use of iodine in toxic adenoma previously untreated with iodine. After a long experience with a considerable series of such cases, I feel that the results following surgical excision were strikingly good. Some years ago I had operated successfully in over 500 cases of toxic adenoma in which preoperative preparation with iodine had not been resorted to. Thereupon a fatality occurred from postoperative hyperthyroidism. My results since the adoption of the preoperative treatment with iodine have been no better. This fact is undoubtedly explained by the increased operative risk following the common indiscriminate use of iodine in recent years.

Cutler and Graham[15] found in a limited series of previously untreated cases of toxic adenoma that a period of primary improvement following the administration of iodine was the rule and not the exception. They also found that their cases of toxic adenoma responded to the iodine in about the same ratio as did the cases of exophthalmic goiter. It may be stated that the average metabolic rate in the 4 cases which they reported was plus 50.5 per cent, indicating a probable high degree of hyperplasia in the adenomata. This fact probably explains the marked improvement following the administration of iodine. The average metabolic rate of patients with toxic adenoma entering the surgical clinic is considerably less than plus 50 per cent, indicating a lesser degree of toxicity and hyperplasia and this fact in turn probably explains the failure in many instances to obtain a decided drop in the metabolic rate or any definite improvement in the clinical status after the administration of iodine. It is undoubtedly true that some of the cases of adenoma with mild degrees of toxicity are either not benefited at all or are made more toxic.

It may be worth while to refer briefly to certain clinical estimates which I made two years ago on the improvement following iodine administration in a series of cases of toxic adenoma, some of which had previously been treated and some that had not been treated with iodine. The results are not given as final but the subjective complaints of the patient and our own clinical impressions are of some value in

judging the results of the therapy employed. Our impressions were based upon estimating the nervousness, tremor, gain or loss of weight and strength, pulse, appetite and often upon the metabolic rate. Of toxic adenoma, previously untreated with iodine, there were 38 cases. Of these cases, after treatment with iodine, 2 per cent were greatly improved; 24 per cent moderately but definitely improved; 29 per cent slightly improved; 29 per cent unimproved and 16 per cent were made worse. In the cases of toxic adenoma, previously treated with iodine, of which there were 41, the results were as follows; after the period of intensive treatment 5 per cent were much improved; 24 per cent moderately improved; 17 per cent slightly improved; 44 per cent unimproved and 10 per cent made worse. It would seem that iodine is beneficial in the cases of active adenoma of higher degrees of toxicity, and that the failures are not of serious moment and occur in the adenomata of lesser degrees of toxicity, which are safe operative risks with or without the previous preoperative treatment with iodine. The instances of failure to obtain satisfactory improvement with iodine are particularly common in that group of cases of toxic adenoma that have been indiscriminately treated with iodine.

### IODINE AND EXOPHTHALMIC GOITER

Marine and Williams,[7] in 1908, after an extensive study of the histological structure and iodine content of the thyroid gland in dogs, and in postoperative and postmortem specimens of the human thyroid gland, stated that iodine causes a reversion in hyperplastic glands to the colloid or resting state in about two or three weeks. They found that, in general, the iodine store in the thyroid varies directly with the amount of stainable colloid and inversely with the degree of active hyperplasia. The thyroid gland has an extraordinary affinity for iodine and the amount than can be stored by any given thyroid varies with the degree of active hyperplasia. In 1924 Plummer[2] published the results of his studies on the effects of the preoperative administration of Lugol's solution in cases of exophthalmic goiter. The results were startling and since 1924 the preoperative preparation of the patient with exophthalmic goiter has come into general use. It was found, and has since been abundantly verified, that when iodine is administered in large doses to the patient previously untreated with iodine, a marked clinical remission is produced. In the course of ten days to two weeks, often earlier, there is produced a striking improvement in the general condition. The weakness, nervousness and appetite are greatly improved. There is a gain of weight, often of 4 to 6 pounds or more. In fact the clinical symptoms of which the patient previously complained may be so mild as to make the patient wonder why operation needs to be undertaken. Accordingly, it is well to acquaint the patient with this remission. Following the administration of iodine there is a fall of 30–35 per cent in the basal metabolic rate. Often the rate returns to normal, whereas in the early cases of hyperplasia and in certain exceptional instances the fall in the rate may be only slight. There is usually a concomitant sharp reduction in the pulse rate. In brief one finds a highly satisfactory improvement both subjectively and objectively in the patient's general condition.

Locally, in the thyroid gland, certain characteristic changes are produced. The gland commonly swells and there is an increase in density due to the rapid accumulation of colloid in the glandular acini. The vascularity diminishes, and the thrills and bruits, characteristically found over the superior thyroid arteries and over the gland itself, may almost entirely disappear. While the explanation for this reduction in vascularity is not clear, one may assume that mechanical pressure upon the vascular spaces within the gland plays a rôle. The reduced activity of the thyroid cells may in some way fail to summon the vascularity characteristic of the pre-iodine phase.

The increased size of the gland is demonstrable by measurements and is apparent to the patient who may complain of a sense of choking or difficulty in swallowing.

Microscopically the hyperplasia, indicative of the activity of the exophthalmic gland, is characterized by tall, columnar cells with large vesicular nuclei and a protoplasm containing, as I have shown, large numbers of mitochondria indicative of cellular activity. These structures are abundantly present in the parenchyma of both toxic adenoma and exophthalmic goiter (Goetsch[16]). There is a rich papillomatous infolding of the acini, which contain a scant amount of colloid and a rich blood supply. Thomas and Rienhoff[17] have shown that this picture of thyroid activity is converted by the iodine into the resting, inactive storage phase of the simple colloid goiter, characterized by large acinar spaces dilated with colloid and lined by low cuboidal or flattened cells with small nuclei. The cystoplasm now contains mitochondria which are much diminished in number and size and which have a reduced staining affinity characteristic of the relatively inactive thyroid. The vascularity is diminished and there may be some increase in connective tissue.

Concomitant with these changes occurring in the thyroid gland, as previously mentioned, there is a clinical remission in the disease following the correct use of iodine in the exophthalmic goiter patient previously untreated with iodine. It is precisely at this period that resection of the thyroid gland is done with a high degree of safety. The mortality following operation in the period of remission in experienced hands has been reduced practically to nil. Dangerous postoperative reactions, formerly not at all uncommon, are rare indeed and the convalescence has become relatively very comfortable indeed. Stage operations are only exceptionally necessary. There is no unusual nervousness or restlessness, the elevation of pulse and temperature is only moderate, there is little if any nausea or vomiting, acetonuria is slight or absent, nourishment is taken promptly and recovery is rapid. In exchange for this satisfactory operative reaction on the part of the patient, the surgeon has accepted some additional technical difficulties. Because of the accumulation of colloid in the gland, the capsule is thinned out by distention; the parenchymatous tissue becomes more fragile and is more easily injured. There may thus be added difficulty in the control of hemorrhage. Because of the increase in size and density of the gland its mobilization, dislocation and general handling may also be more difficult.

In order to produce a favorable remission in the disease, it is essential that iodine be withheld, even in small doses during the preceding weeks or in fact months. Further reference will be made to these facts subsequently. Thus it is customary to administer Lugol's solution (Liquor iodi compositus) preoperatively three times daily in doses of 5–10 minims, or more, depending upon the severity of the case. A remission is commonly produced in five to ten days on the average occasionally two weeks of treatment produce the maximum benefit. The results of treatment are readily appreciated by clinical observations and by frequent determinations of the metabolic rate. The benefit is usually striking. One may encounter the very exceptional case which fails to show any improvement following iodine and which may actually be made worse by its use. It should be mentioned that in certain instances of failure to respond to iodine, the drug may possibly be found to have been administered in a compound prescription and thus to have escaped the notice of the patient. In asking for copies of prescriptions of all medicines taken, I have found potassium iodide, for example, included in a compound prescription which may originally have been for purposes of influencing the cardiovascular system.

An iodine remission may be produced by any form or combination of iodine and the mode of entry into the organism is of

secondary importance. In this connection it is well to mention some advantages possessed by the intravenous administration of iodine under certain conditions. Sodium iodide ampules in daily doses of 10 to 15 grains, may be given intravenously with very satisfactory results. I have found this method particularly applicable in patients with extreme emaciation and with gastrointestinal symptoms such as vomiting and diarrhea. These patients tolerate iodine by mouth poorly and the absorption of the drug from the intestine may be unsatisfactory whether the iodine be given by mouth or per rectum. In such instances a good therapeutic effect with a prompt improvement in the clinical status is assured by the intravenous administration of the drug. This method has also distinct advantages when a more rapid iodinization is desired than might be accomplished by the oral administration of iodine, as for example in the treatment of acute hyperthyroid crisis. Two or three days usually suffice for the control of the acute symptoms. In an occasional case of active exophthalmic goiter previously untreated with iodine, the oral administration is only partially successful. The degree of clinical improvement and the amount of reduction in the metabolic rate may fall just short of the level at which one would feel secure in performing a double lobectomy. Under such conditions the daily intravenous injection of 10–15 grains of sodium iodide for two or three doses produces just enough further improvement to make the bilateral resection entirely safe and free of anxiety for the surgeon. It is also convenient and helpful to add the sodium directly to solutions of glucose which are commonly administered intravenously during the postoperative period. No untoward effects have been observed when the drug was used to the extent of ten daily injections.

It is immaterial whether the preoperative iodine treatment is given by the physician or the surgeon, but for the mutual advantage of all it is highly important that the surgeon, who naturally carries the responsibility of the operation, should have the privilege of observing and studying the patient before the treatment with iodine is instituted. In this manner a better conception is formed of the severity of the disease and the general condition of the patient. A fibrillating and decompensated heart may become regular and compensated under iodine treatment and thus give a faulty impression as to the cardiac reserve. It is not to be expected that in the course of a week or ten days complete recuperation on the part of the heart could have occurred. The extent of the cardiac reserve and the metabolic disturbance may thus be misjudged and thus lead to unfortunate postoperative results.

Reference should be made to the use of iodine after thyroidectomy for acute hyperthyroidism has been performed. The teachings in this regard are that the administration of iodine during the postoperative period is generally advocated with the idea that the postoperative reaction is thereby controlled and that the severity of a possible hyperthyroid crisis is thereby lessened. The use of iodine is continued by some for several weeks or even months following operation with the idea that a recurrence of hyperthyroidism is thereby prevented. It may be of interest to discuss briefly my own views on these teachings. I have not practiced the general use of iodine following thyroidectomy during the last twenty years for a number of reasons. I have felt that as quickly as possible the thyroid remnant should take up its normal function uninfluenced by a drug as potent as iodine and one which has such a profound effect upon thyroid parenchyma. The severity of the postoperative reaction is dependent upon the severity of the antecedent hyperthyroidism and upon the adequacy of the preoperative preparation of the patient. As a result when the postoperative reaction is only moderate or mild there is no danger of a fatality from acute hyperthyroidism, and when the reaction is unusually severe iodine does not control

it and death may result from acute postoperative hyperthyroidism or crisis in spite of enormous dosage of iodine. One does of course resort to any measures calculated to benefit the patient in this crisis and if recovery occurs, it is often and naturally attributed to the administration of iodine. Surgeons have seen patients recover from postoperative crisis and also die from this cause both before and after the general use of iodine postoperatively. The determining factors in the end-result of crisis are the severity of the reaction, physical condition of the patient and especially the cardiac reserve rather than the specific drug that is used. In general it seems that when the postoperative crisis reaches desperate proportions, iodine often fails and in the lesser degrees of postoperative reactions iodine is not necessary. There is of course no harm in its use and it may possibly do some good but all surgeons are familiar with its failure in postoperative crisis in some instances when any beneficial effects would have been most welcome. In fact, the thyroid gland has taken up all the iodine that it can store, has become saturated with it during the preoperative period and any further treatment during the early postoperative period would seem to have no possibility of further effect upon the iodine-saturated gland-remnant remaining after the resection. Furthermore, following some experimental work which we have done in the past two years, it would seem that the adrenal glands play a very large rôle in the hyperthyroid reaction and that this element is not controlled by the giving of iodine, notwithstanding that iodine may have largely controlled the thyroid factor. Again there is no proof whatever that the postoperative administration of iodine prevents the recurrence of thyroid hyperplasia and relapse into a future period of hyperthyroidism. I am very sure that my percentage of recurrence of hyperthyroidism is not greater than that of surgeons who have uniformly practiced the postoperative treatment with iodine.

## INCORRECT USE OF IODINE IN HYPERPLASTIC GOITER

Because of the general use of iodine, often incorrectly prescribed by physicians or advised by the druggist or the laity, untold harm and great suffering are produced in large numbers of patients with exophthalmic goiter. It has become generally recognized that the clinical manifestations of exophthalmic goiter are greatly improved by the administration of iodine given for the first time. It is not generally understood that this benefit is unfortunately only transient. Because of the striking well-being of the patient in the period of remission, the administration of iodine is often interrupted, operation is postponed or reconsidered and the optimum time for surgical intervention is thus allowed to pass. Thereupon after a lapse of four or six weeks to two or three months, there is a return of the symptoms manifest before the institution of the treatment with iodine, and in fact a true clinical exacerbation of the disease may occur and lead to an acute uncontrollable hyperthyroidism resulting even in crisis. When the recurrence of symptoms, often in exacerbated form, becomes apparent to the patient, she frequently leaves her physician or is sent by him to consult the surgeon for what is erroneously considered to be the "last resort," namely operation. Such clinical exacerbation may follow the administration of iodine even in small doses over a period of several weeks to months as well as after the treatment with large doses, which have been interrupted after an indefinite period. In other words, small doses are often more stimulating than the larger ones. The best that can be hoped for in those patients previously treated with iodine and now in exacerbation is the conversion of the active, toxic case into one of moderate severity, and the moderate case into a mild one by the prolonged treatment with large doses of iodine. A state of chronic hyperthyroidism is thus produced and one dare not discontinue the

iodine for it is common experience that relapses occur within a few weeks after the interruption of the iodine treatment. In other words, treatment with iodine once begun had better be continued until such time that operative measures are instituted.

After a critical analysis of the causes of death in a series of 1755 operations for goiter at the Long Island College Hospital during the ten year period from 1920–1929 inclusive (Goetsch),[18] it became evident that the indiscriminate administration of iodine to patients not only with exophthalmic goiter but also with toxic adenoma was a very definitely harmful factor in the causation of the fatalities due to postoperative hyperthyroidism. There were 8 fatalities due to the latter. Six of the 8 fatalities occurred in instances of exophthalmic goiter and 2 followed resection of toxic adenoma. The extent of the operative procedure was not the determining factor in these fatalities for death occurred once after ligation of one superior thyroid artery; once after right hemithyroidectomy which was preceded by two preparatory ligation operations; twice after primary bilateral lobectomy and twice after bilateral lobectomy preceded by preliminary ligation of both superior thyroid arteries. The one fatality following ligation, in a patient who had had no preoperative treatment with iodine, could have been avoided, I feel certain, by the preoperative administration of iodine. This death occurred, however, in 1920 before the preoperative iodine treatment had been generally introduced. The remaining 7 patients had received prolonged treatment with iodine. The majority of these 7 patients received intensive preoperative treatment with iodine. In spite of this fact fatalities occurred after single lobectomy in one instance and after double lobectomy in 4 instances, in 2 of which there had been preliminary ligation operations. It is my definite feeling that the indiscriminate treatment with iodine increased the operative risk and that several of these fatalities would not have occurred had these patients not been previously treated with iodine. I should like to emphasize that the preoperative treatment with iodine does not protect the iodized patient in any way comparable to the protection afforded the patient not previously so treated. The patient suffering with an acute exacerbation following prolonged use of iodine may be a dangerous operative risk whether iodine is given preoperatively or not.

I have observed cases of exophthalmic goiter that have been treated for periods of two to three years by the daily administration of iodine, in fairly large doses. In spite of this prolonged treatment the disease persists in a chronic moderately toxic form and resection is still necessary to obtain relief. The preoperative treatment of patients intended for operation is often wrongly timed, the period of remission, occurring after ten days or two weeks, is allowed to pass and upon the appearance of acute symptoms a few weeks later, the case is referred for operation. This reappearance of acute symptoms is particularly prone to occur if for any reason the administration of iodine is discontinued. During the period of remission, as previously stated, the thyroid gland is usually firm and swollen as a result of the abundant storage of colloid; the thrills and bruits previously present and indicative of a rich vascularity are greatly diminished in intensity or may entirely disappear. During this remission, furthermore, iodine has been stored in the thyroid to the point of saturation. A few weeks after the maximum effects have been produced by the iodine, we often find the thyroid gland again smaller and less firm due to the absorption of the colloid. Meanwhile the rich vascularity of the active gland returns and thrills and bruits are again evident. With this recrudescence of glandular activity the iodine previously stored is metabolized into thyroxin which floods the system with a consequent relapse. The hyperthyroidism, as indicated by the clinical

manifestations and the metabolic rate, may be considerably more severe than before the administration of iodine. At such time the problem for the patient and the surgeon is a graver one, and the operative risk is considerably greater. Surgeons are in a favorable position to observe the ultimate bad results of incorrect treatment with iodine and have accordingly sounded a general warning against the indiscriminate use of iodine. The reports of occasional cures following the use of iodine may be instances of spontaneous recovery for it is known that in rare instances patients with exophthalmic goiter have gotten well without any treatment. Unless iodine is most carefully administered and interrupted at the slightest signs of increased glandular activity, the probability of doing harm is so great as compared with the possibility of doing good that it seems not over-stated to advise against the use of iodine in all medical treatment of exophthalmic goiter.

In patients with Graves' disease who have received iodine sporadically over varying periods of time, who may be either acutely toxic or who may have reached a state of chronic toxic hyperthyroidism, the further intensive treatment with iodine even in large doses usually has little or no beneficial effect. There may be an insignificant fall in the basal metabolic rate. It is most disappointing to compare this unfavorable result with the striking improvement commonly seen when iodine is given for the first time. The failure of the intensive medication with iodine is also seen in instances in which iodine has been previously given as far back as three or four months. It is well recognized that the hyperplastic thyroid gland promptly responds to initial treatment with iodine and that, in subsequent phases of reactivation, it becomes insensitive or refractive to the further administration of iodine even when the drug may have been discontinued for several weeks or months. The post-iodine exacerbation is slow to subside. As a consequence, if one should wish to wait for the subsidence of acute symptoms and for such a time as the thyroid gland would once again become sensitive to the administration of iodine, one might be forced to wait several months as I did a few years ago in a case of a school teacher who was suffering with a very acute post-iodine exacerbation. The purpose in thus waiting for the subsidence of the exacerbation is to avoid possible stage operations. Many patients prefer waiting almost indefinitely to accepting the probability of multiple operations. Occasionally a poor post-iodine effect is noted in a patient who gives no history of medication with iodine. In order to explain this unusual occurrence I have taken particular pains to investigate the past treatment and have usually found that iodine had been given for possibly a few days only, two or three months before, a fact which the patient had entirely forgotten at the time of the first interview.

Oftentimes a difficult problem must be faced by the surgeon when he is consulted by a patient in a phase of acute exacerbation or in a state of toxic chronic hyperthyroidism following prolonged and sporadic treatment with iodine. Further intensive treatment with iodine has relatively little effect either clinically or upon the metabolic rate. In fact the value of the latter as a criterion of the critical nature of the case may be destroyed. The rate may be determined as between +25 and +30 and may thus give to the surgeon a feeling of false security. Operation in such a case may be associated with greater risk of postoperative hyperthyroidism than in a patient who has been treated preoperatively for the first time and whose metabolic rate may be as high as +35 to +40. Too much reliance should therefore not be placed upon the metabolic rate in such instances. If all treatment with iodine is discontinued, the symptoms may become even more severe and the patient may thus be condemned to a further prolonged period of acute suffering. One may thus be forced to administer iodine in

large doses hoping to produce thereby a toxic chronic hyperthyroidism. In this state, as in the post-iodine exacerbation, the dangers of postoperative hyperthyroidism following a bilateral resection operation may be very great and as a consequence the surgeon is forced to resort to stage operations, such as ligations of the thyroid arteries and single lobectomies. It has been my custom under these conditions to discontinue iodine and to wait for a period of several weeks during which time sedatives are administered. Thereupon, ligation of the thyroid arteries is done without the preceding administration of iodine. A period of two to three months without iodine is then allowed to elapse following which iodine is again intensively administered. At this time the thyroid gland once more responds, a definite clinical improvement follows and the double lobectomy is carried out. In this manner the clinical improvement produced by the iodine together with the previous benefit following ligation make it possible to perform double lobectomy with a minimum of risk. I have thus often performed preliminary ligation as the first stage in preference to single lobectomy because the double lobectomy in one session subsequent to ligation is somewhat safer and more satisfactory than when double lobectomy is done as a two-stage operation. If a single lobectomy is performed as the first stage in a case of acute hyperthyroidism following treatment with iodine, the iodine is continued throughout the postoperative period and until the second lobectomy is performed. In this manner an acute exacerbation of symptoms resulting from the excessive secretion of thyroxin elaborated from the iodine store in the second lobe is avoided.

## SUMMARY

Iodine has an important relationship to the normal function of the thyroid gland in which it is constantly present and is stored as a normal constituent.

Simple colloid goiter, the inactive type of parenchymatous goiter, commonly develops whenever there is a deficient intake or a faulty metabolism of iodine in the body. Simple colloid or endemic goiter may be prevented by the prophylactic administration of minute amounts of iodine. Iodine, in small amounts, together with small amounts of thyroid extract is advised in the treatment of simple goiter. This is the only type of goiter in which the therapeutic administration of iodine is indicated. The prolonged administration of iodine to the simple colloid goiter may however occasionally stimulate the gland with the consequent production of hyperthyroidism. A correct diagnosis as to the type of goiter is therefore of the greatest importance in order to institute correct therapy.

A non-toxic goiter may be activated and the symptoms of a toxic goiter may be exacerbated by the indiscriminate administration of iodine.

The administration of iodine during pregnancy is indicated only in case inactivity of the thyroid gland is present. The physiologically overactive thyroid gland in pregnancy may be stimulated to further activity resulting in a state of true clinical hyperthyroidism.

The administration of iodine does not prevent the growth and development of true adenoma and has no place in the medical treatment of this condition. Nontoxic adenoma is commonly activated by indiscriminate treatment with iodine and the symptoms of toxic adenoma are exacerbated by its use. The preoperative intensive preparation of the majority of patients with toxic adenoma does not produce improvement comparable to that seen in the case of exophthalmic goiter. The acutely toxic adenomatous goiter particularly when the metabolic rate is high, is often favorably influenced by the use of iodine, whereas those cases of adenoma with lesser degrees of hyperthyroidism may show relatively little improvement. An appreciable number in this group may be made acutely worse.

The hyperplastic thyroid gland has an extraordinary affinity for iodine which causes the hyperplasia to revert to the colloid or resting state. Accordingly when iodine is intensively administered to the patient with Graves' disease, previously untreated with iodine, a marked clinical remission in the course of the disease is produced. Operation should be and can be safely performed during this period of remission. The mortality of resection operations done during the period of remission has been reduced almost to nil, and stage operations are rarely necessary. If thyroid resection is not done at this favorable time of remission, the patient often relapses into a state of clinical exacerbation in the course of one to two or even three months. A condition of uncontrollable hyperthyroidism may thus result. Similarly, exacerbation may follow upon the administration of iodine even in small doses, over a prolonged period.

The hyperplastic thyroid gland in the phase of reactivation following a previous period of treatment with iodine becomes relatively insensitive or refractive to the further administration of iodine. The preoperative treatment with iodine does not protect the iodized patient with toxic adenoma or Graves' disease in any way comparable to the protection afforded the patient not previously so treated. The patient suffering with an acute exacerbation following prolonged use of iodine may be a dangerous operative risk whether iodine is given preoperatively or not. It is particularly in these circumstances that recourse must be had to multiple operations such as preliminary ligation and single lobectomies to eliminate the increased risk involved in a primary double lobectomy.

Iodine has little effect in controlling postoperative hyperthyroidism. There is no evidence that the postoperative administration of iodine reduces the incidence of recurrent hyperthyroidism. The spontaneous hyperthyroid crisis occurring occasionally in the course of severe Graves' disease may be effectively controlled by large doses of iodine given either orally or intravenously. When the crisis occurs as a result of the incorrect use of iodine, the further administration of iodine, even in large amounts, is ineffectual and a fatal outcome may ensue.

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# THE UPPER URINARY TRACT DURING NORMAL PREGNANCY*

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NUMEROUS investigations of the urinary tract during pregnancy have been made, notably those of Kretschmer and Heaney,[7] Carson,[2] Hofbauer,[6] Seng[9] and Baird.[1] Until recently one has been handicapped in conducting an investigation of the upper urinary tract during pregnancy, because of the possibility of exciting trouble which these patients tolerate so poorly. With the advent of the newer intravenous preparations the urinary tract lends itself readily to investigation with the assurance that no harm will come of the procedure.

While the theory that mechanical obstruction is the major cause is not new, it has usually been passed over lightly and a search made for some more occult cause. Among the causes usually given are hypertrophy of the lower ureter and the various disturbances of internal secretion.

Cruveilhier[4] in 1841 found dilatation of the ureters in women who died during the latter months of pregnancy. Craigin[3] in 1918 first pointed out the preponderance of right-sided dilatation. Hofbauer[6] in a paper published in 1928 made the following statement. "A moderate degree of hydroureter is at present considered an almost constant concomitant of pregnancy." He also pointed out that a definite hypertrophy of the musculature and connective tissue, especially pronounced in the juxtavesical portion of the ureter, was constant. Angulation of the right ureter at the distal end of the juxtavesical portion, due to the dextro-rotation of the pregnant uterus, he gave as the cause of right-sided preponderance. The atony of the upper ureter he explained by the increased bile-acid content of the blood in pregnant women. Carson[2] stated that "the sigmoid seems to protect the left ureter to some extent" and dismissed the subject. Seng[9] in 1929 reported a series of bilateral instrumental pyelograms in 78 pregnant women. His conclusions are in accord with this presentation as to occurrence and frequency, but no mention is made of the causative factor. Gremme[5] concluded there was an atony of the upper urinary tract that allowed compression, which resulted in dilatation. Opitz[8] was the first to call attention to the compression of the ureters at the pelvic brim. Baird[1] in November 1932, after most of the work in this presentation had been compiled, analyzed 1000 cases with the following conclusions:

(1) Pregnant women show varying degrees of atony of the upper urinary tract. In some this is very slight so that no appreciable stasis is produced. In others it is very marked and can be shown to occur at the very beginning of pregnancy. (2) In the second half of pregnancy, dilatation and stasis frequently result and are due to pressure of the uterus on the atonic ureters at the pelvic brim. (3) Dilatation and stasis from the pelvic brim upwards can be produced in the nonpregnant by ovarian cysts. In these the dilatation is less and there is an absence of the marked elongation and kinking of the ureters which is characteristic of pregnancy, even although the pressure exerted by the cyst may be greater than could be exerted by the pregnant uterus. The atony peculiar to pregnancy is therefore the primary factor. (4) In normal pregnancy the tone of the ureters has been shown to improve near term, and in cases of the albuminuric toxemia there

* This work was done in the departments of Urology and Roentgenology of the Youngstown Hospital Association, Youngstown, Ohio. Part of the work was made possible by Winthrop Chemical Company in supplying us with the necessary Neo-Skiodan. Read at the Reunion of Former Interns of Rhode Island Hospital.

is a minimum of atony and stasis. In both instances there is believed to be an excess of posterior pituitary hormone in the blood. The primary factor in the production of the changes in the upper urinary tract in pregnancy is probably, therefore, a disturbance of the endocrines. (5) Infection of the urinary tract is common during pregnancy and is often unrecognized. (6) Infection is always preceded by stasis and seldom clears up completely until the stasis is relieved by termination of the pregnancy. (7) Early diagnosis is most important, as if instituted early, simple treatment by abundant fluids and alkalis is sufficient to enable the patient to go to term. (8) Ureteral catheterization has a definite place in the treatment of serious cases for the relief of pain and the promotion of drainage.

Our attention was focused on the relation of the ureters, sigmoid and the gravid uterus at the pelvic brim by an autopsy at term. No claims of originality or priority are made. Our reason for presentation of the subject is to emphasize the mechanics producing the dilatation.

After satisfying ourselves that the chief factor in the production of dilatation was a mechanical one, we then became concerned with the various elements producing it. We do not disregard the congestion during pregnancy, or the possible disturbance of the various internal secretions. We will show, by means of a series of studies with the aid of the roentgen-ray and intravenous substances, that the pressure of the gravid uterus on the ureters as they cross the bony brim of the pelvis is the chief factor. The reason for right-sided preponderance is found in the protective cushion of the sigmoid, interposed between the left ureter and the uterus.

If the hypertrophy of the juxtavesical portion of the ureter, described by Hofbauer,[6] is the most important factor, is it not reasonable to assume that the dilatation will begin immediately above this point? Our evidence shows that the pelvic ureter does not enter into the process of dilatation. Only that portion of the urinary tract above the pelvic brim shows the dilatation. If disturbed internal secretions or toxins are productive of the change, why do they act more directly on the right side? We present a logical explanation of the phenomenon. Gremme,[5] in placing the atony before the dilatation, we believe, puts the cart before the horse. We know that occlusion of the ureter by stone will produce dilatation with its resulting atony above the stone. This atony persists, after the stone has been removed, for a period of time in direct proportion to the completeness of the block and the length of time it has existed. Contrary to the belief of Baird,[1] we have shown elongation and tortuosity of the ureters in the presence of cysts of the ovaries and fibromas of the uterus. The improvement near term noticed by Baird[1] and interpreted by him as due to an excess of posterior pituitary hormone, we are convinced is due to the change in position of the uterus as it rises in the abdominal cavity.

If the prime factor is a mechanical one, then masses such as uniform fibromas of the uterus and ovarian cysts of a size comparable to the pregnant uterus, will produce similar effects. That this occurs we will show by a series of studies of the upper urinary tract in these conditions. Finally, if the causative factor is mechanical pressure, the phenomenon should be absent in the quadruped. So far dilatation of the upper urinary tract in pregnant animals has not been shown.

The work herein presented consists of studies of the upper urinary tract during normal pregnancy. Intravenous urography was the medium of investigation. It was selected for two reasons: (1) It presents the unaltered physiology of the dynamics of expulsions without the added distortion of instrumental irritation. (2) It is a safe method, with conditions ideally suited to it. Cases selected for study were included only when the patient was free of both signs and symptoms of urinary disturbance. A faint trace of albumen, a few leucocytes, or an occasional small clump of leucocytes in the voided specimen was allowed. Primipara to para ix were included. The

period of gestation ranged from the third month to term. The ages of the patients were from fifteen to forty-two. The intravenous substances used were skiodan, neo-iopax and neo-skiodan.

### ANALYSIS OF THE MATERIAL

The material collected consists of 52 cases of normal pregnancy, of which 49 are included in the analysis. Three were discarded because the urinary tract was insufficiently visualized to permit classification. The dilatation of the upper urinary tract was graded from 0 to 4. The anatomical divisions considered were the ureters, pelves and the calices. A grade 4 dilatation of the ureter equals the calibre of the undistended small gut. A grade 4 pelvis is comparable to a grade 4 hydronephrosis. A grade 4 calix is read when the normal contour of the calix is completely obliterated.

Analysis of the three tables: position of the fetus (Table I), number of pregnancies (Table II) and the period of gestation (Table III) shows these factors to exert little, if any influence, with the exception of the period of gestation, where it will be noticed there is an increase in the percentage of cases showing the higher grades of dilatation during the sixth, seventh and eighth months of pregnancy. Selecting the groups showing the highest incidence of grade 3 and 4 dilatation on the right side

TABLE I
POSITION OF FETUS; GRADE OF INVOLVEMENT

| *Position* | | *Right* | | | | | *Left* | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Per Cent* | 0 | + | ++ | +++ | ++++ | 0 | + | ++ | +++ | ++++ |
| Occiput rt | 32 | 2 | 0 | 6 | 10 | 14 | 8 | 10 | 12 | 0 | 2 |
| Occiput lt | 24 | 2 | 0 | 8 | 10 | 4 | 12 | 8 | 2 | 2 | 0 |
| Occiput tr | 12 | 0 | 2 | 6 | 0 | 4 | 6 | 0 | 4 | 2 | 0 |
| Breech | 6 | 0 | 2 | 0 | 0 | 4 | 0 | 4 | 2 | 0 | 0 |
| Twins | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 |
| Undetermined | 22 | 4 | 2 | 2 | 8 | 6 | 10 | 4 | 4 | 4 | 0 |
| | Per Cent | 8 | 6 | 22 | 30 | 32 | 36 | 26 | 26 | 8 | 2 |

TABLE II
NUMBER OF PREGNANCIES; GRADE OF INVOLVEMENT

| *Para* | | *Right* | | | | | *Left* | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Per Cent* | 0 | + | ++ | +++ | ++++ | 0 | + | ++ | +++ | ++++ |
| i | 18 | 2 | 0 | 10 | 4 | 2 | 8 | 6 | 0 | 4 | 0 |
| ii | 26 | 0 | 0 | 6 | 6 | 14 | 8 | 4 | 12 | 2 | 0 |
| iii | 12 | 2 | 2 | 0 | 4 | 4 | 4 | 4 | 4 | 0 | 0 |
| iv | 18 | 0 | 2 | 4 | 4 | 8 | 4 | 10 | 4 | 0 | 0 |
| v | 8 | 2 | 0 | 0 | 4 | 2 | 2 | 0 | 4 | 0 | 2 |
| vi | 6 | 0 | 0 | 0 | 4 | 2 | 2 | 0 | 2 | 2 | 0 |
| vii | 6 | 0 | 2 | 2 | 2 | 0 | 6 | 0 | 0 | 0 | 0 |
| viii | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 2 | 0 | 0 | 0 |
| ix | 2 | 2 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 |
| | Per Cent | 8 | 6 | 22 | 30 | 32 | 36 | 26 | 26 | 8 | 2 |

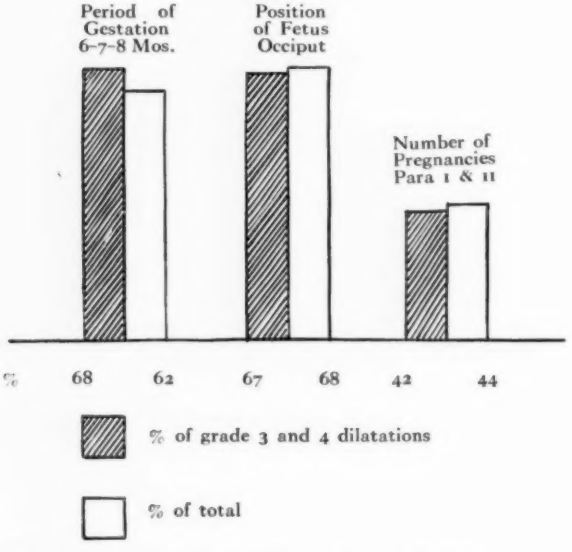
(Table IV), it will be seen that they maintain a proportion in the greater degrees of dilatation, practically identical to their proportion of the whole, with the exception of the period of gestation already mentioned.

TABLE III
PERIOD OF GESTATION; GRADE OF INVOLVEMENT

| *Period* | | *Right* | | | | | *Left* | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Months* | *Per Cent* | 0 | + | ++ | +++ | ++++ | 0 | + | ++ | +++ | ++++ |
| 3 | 6 | 0 | 2 | 0 | 4 | 0 | 2 | 2 | 2 | 0 | 0 |
| 4 | 10 | 2 | 0 | 8 | 0 | 0 | 8 | 0 | 0 | 2 | 0 |
| 5 | 8 | 2 | 0 | 2 | 0 | 4 | 4 | 2 | 0 | 2 | 0 |
| 6 | 16 | 0 | 0 | 4 | 4 | 8 | 4 | 2 | 8 | 0 | 2 |
| 7 | 24 | 2 | 2 | 0 | 10 | 10 | 8 | 4 | 12 | 0 | 0 |
| 8 | 22 | 2 | 2 | 8 | 4 | 6 | 6 | 10 | 4 | 2 | 0 |
| 9 | 12 | 0 | 0 | 0 | 8 | 4 | 4 | 6 | 0 | 2 | 0 |
| | Per Cent | 8 | 6 | 22 | 30 | 32 | 36 | 26 | 26 | 8 | 2 |

Thus the group including the sixth, seventh and eighth months of pregnancy constituted 62 per cent of the total, whereas

TABLE IV


Period of Gestation 6-7-8 Mos.
Position of Fetus Occiput
Number of Pregnancies Para I & II
% 68 62 67 68 42 44
% of grade 3 and 4 dilatations
% of total

the grade 3 and 4 dilatation of this group comprise 68 per cent of all grade 3 and 4 dilatations. The cases showing the occiput in presentation constitute 68 per cent of the total, and the grade 3 and 4 dilatations of this group comprise 67 per cent of the total grades 3 and 4. Para i and ii constitute 44 per cent of the total and grades 3 and 4 in the same group comprise 42 per cent of all grades 3 and 4. Para i, ii, iii and iv constitute 74 per cent of the total, and again in the same group the grades 3 and 4 comprise 74 per cent of the total grades 3 and 4. It is therefore evident that in this series position of the fetus and number of pregnancies have no bearing on the production of upper urinary dilatation. However, there is an increase in the greater degrees of dilatation during the sixth, seventh and eighth months of pregnancy.

Of the 49 cases showing sufficiently clear outlines of the upper urinary tract to allow their classification as to dilatation of the ureters, pelves and calices 4 or approximately 8 per cent show no dilatation of the upper urinary tract (Table V);

TABLE V
INVOLVEMENT

| *Sides* | *Per Cent* |
|---|---|
| Both sides | 52 |
| Right | 40 |
| Left | 0 |
| Neither | 8 |

26 or 52 per cent show involvement of both sides; 20 or 40 per cent show the right side alone involved, and in no case was the left side alone involved. In other words, 92 per cent of all the cases studied show some dilatation of the upper urinary

tract. In only one case was the dilatation of the left side read as a grade 4 and in that case the mid-ureter was the portion showing the greatest involvement.

In no case was a markedly dilated pelvic ureter shown. However, several rather tortuous pelvic ureters were shown. Visualization of the pelvic ureter was not constant, but the left side was shown more frequently than the right. In 23

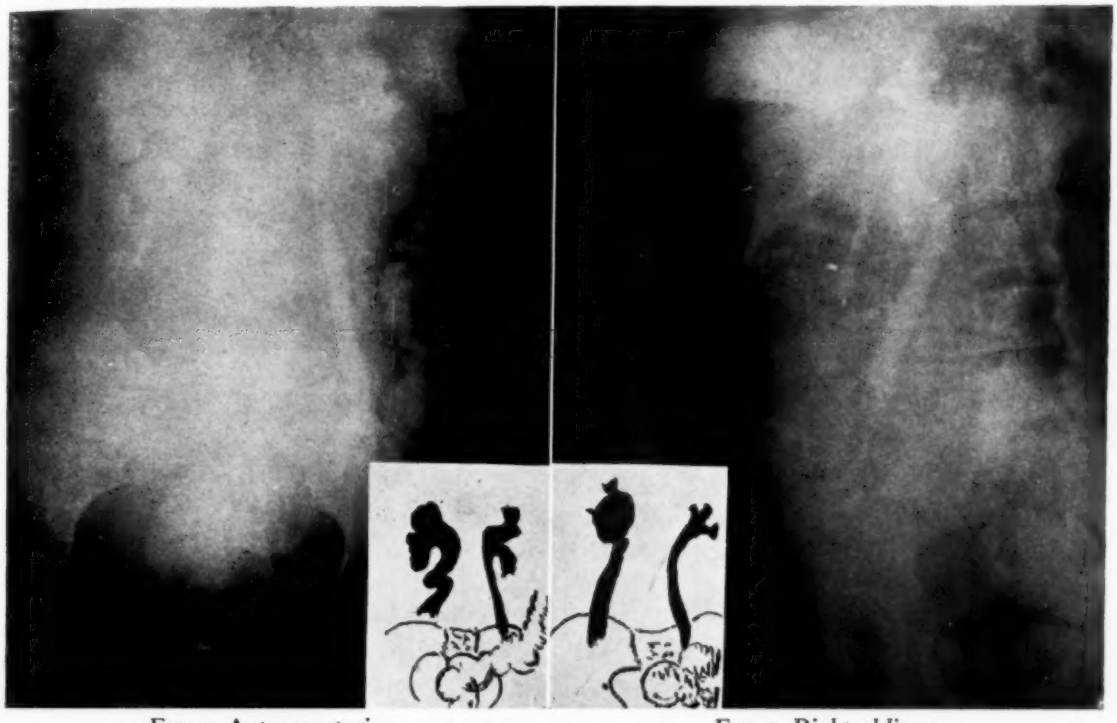


Fig. 1. Anteroposterior.



Fig. 2. Right oblique.

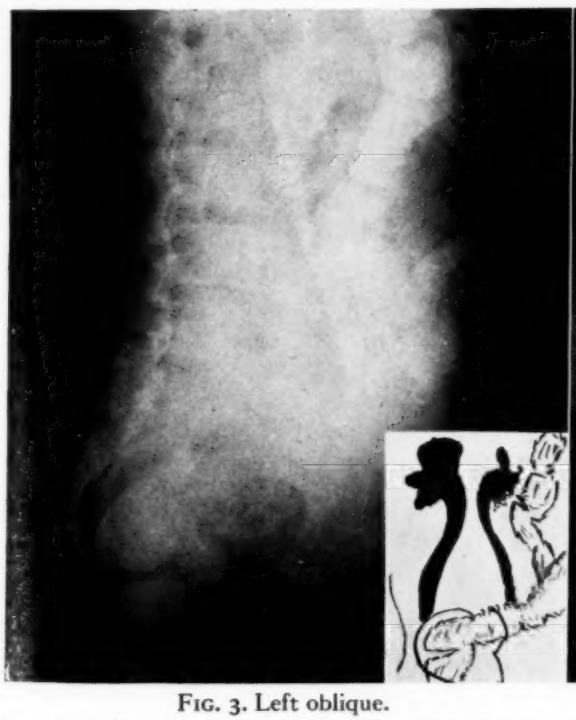


Fig. 3. Left oblique.

Fig. 4. Anteroposterior oblique.

Figs. 1–4. Reproductions made with combined opaque enema and intravenous delineation of urinary tract.

cases or approximately 46 per cent neither pelvic ureter was shown (Table VI). In 34 per cent the left alone was shown. In 10 per cent both were visible and in 8 per cent the right alone was demonstrated, one of these in a patient showing a marked deformity of the bony pelvis.

Inasmuch as the dilatation was in all cases limited to that portion of the urinary tract above the pelvic brim, it is obvious

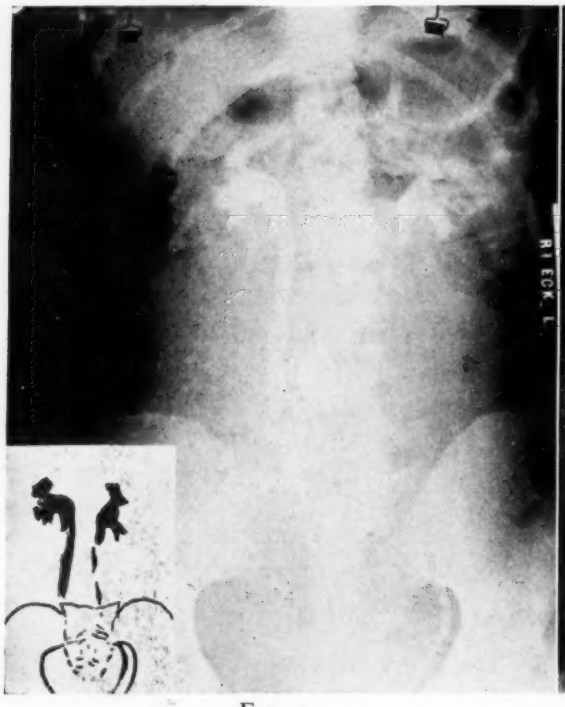


FIG. 5.

FIG. 6.

FIGS. 5 and 6. Reproductions showing effect on upper urinary tract of cysts and tumors.

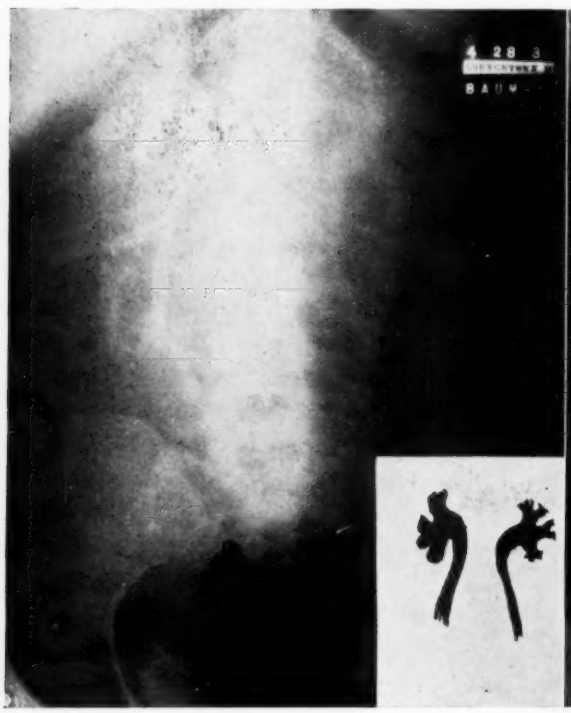


FIG. 7.

FIG. 8.

FIGS. 7 and 8. Reproductions of 2 typical cases of normal pregnancy.

that the hormonal element is not the factor of chief importance. Concerning hypertrophy of the lower ureter we have insufficient pathological data to consider the subject except from its clinical aspect. The pelvic ureters we have shown have been neither dilated nor contracted to any appreciable degree.

Table VI

VISUALIZATION OF PELVIC URETERS

| *Side* | *Per Cent* |
|---|---|
| Neither | 46 |
| Left | 34 |
| Both | 12 |
| Right | 8 |

At operation and autopsy it is quite evident that the ureter is subjected to considerable pressure at the pelvic brim as the pregnant uterus rests quite intimately on the posterior wall. The interposition of the sigmoid between the uterus and the left ureter is not only evident, but constant. The relation is well shown in a series of reproductions made from roentgenograms (Figs. 1–4) the patient having been given the intravenous substance to dilineate the urinary tract, and the lower bowel injected with a weak suspension of barium. In the anteroposterior view (Fig. 1) the sigmoid can be seen to cross the ureter in the region of the left sacroiliac joint. Views in the right oblique (Fig. 2) show the right ureter and the right sacroiliac joint free from contact with the bowel. Views in the left oblique (Fig. 3) show the more intimate relation of the sigmoid, left ureter and left sacroiliac joint. Anteroposterior obliques (Fig. 4) with the target at a perpendicular to the pelvic inlet, will complete the demonstration of the interposition of the sigmoid. The sigmoid not only acts as a buffer to the left ureter, but by exerting a forward thrust on the left side of the pregnant uterus adds to the already increased pressure on the right.

In the presence of tumors of the uterus and cysts of the ovary (Figs. 5 and 6) very definite obstruction to the ureters at the pelvic brim is shown. These findings are neither as marked nor as constant as in the cases of pregnancy (Figs. 7 and 8). This is easily explained as one seldom finds a symmetrical fibroma of the uterus or a cyst of the ovary the size of a late pregnancy. In the series of tumors and cysts presented all have been operated on and the diagnosis proved. No case is included in which there was a nodular or irregular mass exerting direct pressure on the ureters. The illustrations exhibit all the cardinal features shown in the series of pregnancies. Throughout the series the ureters are shown above the pelvic brim. There is a marked widening of the space between the ureters. All grades of dilatation are shown. All three anatomical parts, the ureters, pelves and the calices are involved. There is a definite preponderance of right-sided dilatation.

## SUMMARY

1. Dilatation of the upper urinary tract accompanies normal pregnancy as a result of mechanical pressure exerted by the pregnant uterus on the ureters as they cross the pelvic brim.

2. The position of the fetus or the number of pregnancies does not influence the degree of dilatation.

3. The period of gestation, due to the size and position of the uterus, influences the degree of dilatation to some extent, the greater degrees of dilatation occurring during the sixth, seventh and eighth months of pregnancy.

4. Right-sided preponderance is due to the protection of the left ureter by the sigmoid, plus the added pressure on the right as a result of the forward thrust exerted by the sigmoid on the left side of the uterus.

5. Uniform fibromas of the uterus and ovarian cysts produce the same phenomenon.

Acknowledgment of the cooperation of the various members of the Staff of Youngstown Hospital, too numerous to mention, for their kind help in referring us the necessary cases is hereby made.

[For References see p. 465.]

# THE DANGER OF SUDDEN DEFLATION OF ACUTELY DISTENDED BOWEL IN LATE LOW INTESTINAL OBSTRUCTION*

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IN a previous communication[1] from this clinic the idea was expressed that in certain late cases of low intestinal obstruction rapid deflation of the acutely distended bowel may be responsible for a rapidly fatal outcome. While such a causal relationship has been suggested by a few previous writers there is still considerable doubt and misapprehension among surgeons as to its importance. The purpose of this paper is to assemble the reported evidence as well as present additional data bearing on the validity of this assumption. Its probable mechanism will also be discussed. The application to the treatment of these late cases is obvious.

## PREVIOUS OBSERVATIONS

It is an old observation that following the successful relief of a simple mechanical obstruction such as by cutting an adhesion, within a few hours the patient may become much worse and die.

The earliest instance which I could find was reported in 1887, by Schede[2] who described the case of an eighteen year old boy upon whom he operated on the eighth day after the onset of symptoms. A ligamentous band obstructing the mid-ileum was found and cut. The dilated bowel emptied into the collapsed bowel and indeed the patient had several bowel movements shortly afterward. Nevertheless he died with increasing "cardiac weakness" twenty hours after the operation.

J. B. Murphy[3] described a similar case in 1897, in which the patient died nine hours after the successful relief of the cause of the obstruction. The frequency of such experiences are difficult to determine, although most authors mention their occurrence. A recent example was reported by Heusser and Schar.[4]

The usual reason given for death following such apparently successful operations is that the toxic contents of the obstructed bowel, gaining access to the healthy bowel below the occlusion, are rapidly ("greedily" is the word used by some) absorbed and kill the patient. Contrary to such an inference is the observation that the same lethal result may follow in cases where the obstructed toxic contents are drained to the outside.

Such an instance was described by Britton[5] who operated on a twenty-five year old man five days after the onset of symptoms. An inch long opening was made into the dilated bowel and the edges sutured to the abdominal wound. A large amount of liquid feces and gas escaped. Immediate recovery was good, but a little later the patient became restless and died eight hours after the operation. Autopsy showed only a kink in the small intestine below a Meckel's diverticulum as the cause of the obstruction.

Though no proof is cited that such a toxin can be absorbed from normal bowel, so firmly entrenched is this idea that one of the important operative procedures recommended by many authors is the thorough evacuation of the obstructed bowel through a temporary enterostomy tube in order to "rid the body of the toxic contents."

This prevalent idea overlooks the important experiments of Wilkie[6] who, twenty years ago, showed that toxic contents are not absorbed from normal gut, an observa-

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tion which has been confirmed by others since. He expressed the belief that sudden death following the relief of the distention in late cases of low obstruction could occur because the intestinal capillaries, being paralyzed and dilated, allowed the loss of much blood and fluid into the splanchnic area. He recommended, therefore, the giving of large quantities of saline. This measure has proved ineffective in low obstruction, though it is of additional interest to note in *high obstruction* that Wilkie in Scotland, at about the same time as Hartwell and Hoguet[7] in this country, observed that saline and glucose injections exerted a beneficial effect as shown by a prolonged survival time, a now well-understood phenomenon which rests on well-established and extensively confirmed evidence.

In the same year (1913) Murphy and Brooks,[8] among a large number of experiments on dogs, reported one on the effect of distention.

A loop of bowel was distended up to a pressure of about 70 mm. Hg with "toxic contents" obtained from a seventy-two hour obstructed loop of another dog. Thoracic duct lymph (75 c.c.) was collected for six hours at which time the dog died. The material was then injected into another intact dog who vomited and had other symptoms, but recovered. Unfortunately no observations were made as to the effect of sudden release of this high pressure. The possibility was apparently overlooked, moreover, that absorption of toxic material in this experiment may have occurred into the blood stream and not into the lymphatics, and may have been extensive enough to have caused the death of the animal.

For the next ten or fifteen years one finds little interest shown in the present question until 1926, when H. B. Stone[9] in a short abstract recorded the following belief:

Surgical relief of the obstruction and the evacuation of bowel contents . . . hasten the generalized dissemination of the toxins in the bowel wall for . . . the relief of obstruction and the consequent fall of intra-intestinal pressure permits a rapid return of circulation through the tissues of the bowel wall and with this revived circulation comes a rapid carrying off through the general blood stream of the poisonous substances in the bowel wall.

Some experimental observations were cited in support of this idea.[10]

In one series of dogs, India ink placed in closed loops did not escape the lumen, except where reconstitution of the intestine took place spontaneously. In these animals the black granules were found in the regional lymph glands draining the loop. In other experiments detached segments of bowel containing toxic contents were immersed in Ringer's solution. Only when the loop was alternately distended and collapsed by applying intermittent pressure to the lumen could the passage of poisonous material through the wall be demonstrated. This was shown by the production of symptoms on injecting the Ringer's solution into intact dogs.

In a clinical address[11] on the "Significance of Recoil following Visceral Decompression," Wheeler, in discussing intestinal obstruction, expressed the opinion that "acute cases did best when a slow steady drain of intestinal contents could be established through a small tube." Bad results were encountered often when "the distended intestines were emptied as completely as possible at the time of operation by the use of a large tube," and "rapid drainage through a Paul's tube . . . may be followed by deplorable results." He went on to state that "the sudden relief of the distended abdomen and the collapse of the intestinal walls, together with the flooding of the vascular channels and the fall in blood pressure, produce the clinical picture of shock." No cases were described. Morton[12] reported operations in which deleterious results followed complete evacuation of obstructed bowel stating that "stripping of bowel is a very dangerous procedure." Löwen[13] in dogs and rabbits demonstrated a drop in blood pressure and occasionally death after "stripping" obstructed bowel especially of several days' duration.

Gatch[14] after stating that there is "danger from the too sudden relief of intra-intestinal pressure above an obstruction . . . " described some experiments on the effect of pressure on absorption.

A closed loop of small intestine was distended outside the abdomen until the pressure was equal to systolic blood pressure. A large dose of nicotine or KCN was introduced into the loop; no absorption took place. The pressure was then lowered until it was about half of the systolic pressure, whereupon a rapid absorption of the poison occurred as shown by a sudden marked increase of blood pressure in the case of nicotine or the respiratory stimulus in case of KCN. If such a loop was distended while inside the abdomen absorption occurred at the high pressure, indicating a transperitoneal pathway.

Wangensteen and Loucks,[15] on the other hand, state that they obtained no evidence of absorption of histamine placed in a closed segment of bowel distended to a pressure of 80 mm. Hg while inside the abdomen. The difference is probably partly due to the fact that nicotine and KCN are normally absorbed by intestinal mucosa whereas histamine is not. Dobyns and Dragstedt[16] on the other hand in "crossed" experiments also failed to observe transperitoneal transmission with high pressures even of nicotine, except in two of five dogs, and in them the loop was not viable.

Heusser and Schar,[4] impressed with the sudden death which occurred in a child with low obstruction after simple release of the adhesion causing it, performed experiments on rabbits.

They produced strangulated closed loops and in twenty-four hours injected into the distended loop thus produced a fatal dose of strychnine; nothing occurred although they waited one hour. They then released the ligature causing the strangulation; spasms developed within twenty minutes and a typical strychnine death occurred ten minutes later.

Wangensteen and Loucks[15] in all but one of eleven dogs noted a drop in the blood pressure after releasing a strangulated obstruction. This effect was noted even in strangulations of one-half hour duration, but the drop was greater when a strangulation two or three hours old was released.

The present author has recently had two cases of neglected strangulated hernia in which transient severe shock followed immediately after the tight neck of the sac was cut.

## PRESENT OBSERVATIONS

The following observations, made in this clinic, while casual and diverse, have a bearing on the problem at hand. They confirm the observation already discussed that sudden deflation of the distended bowel may be followed by serious symptoms and often a lethal outcome. They suggest, too, a causal connection between the two events. They also point to the fact that the effect is probably due to the sudden access into the circulation of some toxin or infection.

1. *"Toxic" Symptoms and Death after Release of an Obstructing Band:*

CASE I. A young well-nourished negro was admitted to Barnes Hospital several years ago, and was operated on for intestinal obstruction of several days' duration. A single band occluding the terminal ileum was found soon after opening the abdomen. It was cut and obstructed contents passed readily into the collapsed bowel. The wound was closed without doing anything further. I saw the patient several hours later and he was thrashing about in bed, delirious and irrational, with a vigorous rapid bounding pulse and a fever of 40°c. He appeared overwhelmed by some profound intoxication and died shortly afterwards. No autopsy was obtained.

2. *Toxic Symptoms and Death after Resection of Gangrenous Bowel:*

CASE II. J. S. (No. F1524), a well-nourished white child, aged four years, was admitted to the St. Louis Children's Hospital, July 24, 1929, three days after the onset of acute abdominal symptoms. Aside from dehydration the general condition of the child was good. Adequate parenteral fluid was given. At operation under ether anesthesia I found, 8 inches

above the ileocecal valve, an irreducible gangrenous intussusception of the terminal ileum which I resected, then closed the ends and did a lateral anastomosis. An enterostomy tube was introduced above as a safety valve although obstructed contents were already draining into the collapsed bowel. The child bore the operation well and at its conclusion the circulation and color were good and remained so for about six hours. Then rather suddenly there was a profound change. Her pulse, which was normal in volume, about 100 in rate, became bounding, irregular and too rapid to count. Subcutaneous and intravenous fluids were administered without apparent effect. Her behavior was that of a patient who had suddenly had a tremendous infection thrown into her circulation. She became first restless, then excited and finally had to be restrained. She then lapsed into coma. The temperature rose rapidly and was recorded as 42°C. just before death which occurred ten hours after operation. The autopsy showed an intact anastomosis with no leakage. The peritoneum was clear. The obstructed bowel was still somewhat distended and showed the usual changes of cyanosis and edema and on section showed loss of mucosa and focal necrosis of the gut wall. It seemed apparent that toxic products of the necrotic mucosa of the ileum or its contents had been absorbed into the portal vein rather than through the peritoneum and that the fall of intra-intestinal pressure from drainage through the anastomosis and enterostomy had hastened it. It seemed likely too that if more of the obstructed bowel had been resected the portal of entry of toxins might have been removed, although, from inspection at operation, the obstructed bowel seemed entirely viable. This point will be discussed later on.

3. *"Toxic" Symptoms after Spontaneous Relief of Obstruction:*

Case III. M. D., (No. J221), a four months old infant, was admitted to St. Louis Children's Hospital on January 23, 1933, with a three-day history and signs of intussusception. Aside from dehydration for which adequate parenteral fluid was given the general condition was good. At operation I found practically the entire colon invaginated into the sigmoid, which, however, was rather easily reduced. The ileum itself above the intussusception was tremendously dilated, cyanotic in color and showed several dark areas opposite the mesenteric attachment which looked like beginning gangrene. The edema at the ileocecal valve, which was part of the intussusception, was so marked that after reduction none of the obstructed contents in the ileum passed into the cecum. An enterostomy was therefore decided upon and performed with a small mushroom catheter in a high loop of ileum with a good circulation. The tube was brought through a separate stab wound and drained gradually. Recovery was complicated by a wound infection, otitis media, and a pneumonia but was eventually complete. The enterostomy tube came out in a week, drainage ceased and the wound healed. One month later, however, sudden distention and vomiting developed and a diagnosis of intestinal obstruction was made. Shortly afterward the nurse, while bathing the baby, saw the enterostomy wound suddenly open and a large amount of gas and liquid feces escape with almost explosive force all over the bed. The distention was immediately relieved, but the infant went into shock. Its skin took on a bluish pallor, the hands and feet became cold, the pulse feeble and very rapid and the pupils dilated and eyeballs rolled upward. After about five or ten minutes these signs gradually disappeared and the baby went on and made a complete recovery. The enterostomy wound closed promptly and no further complications have developed up to the present (April 1934).

4. *Increase of Pulse Rate after Sudden Drainage of Distended Bowel:*

Case IV. A young negro with serious luetic heart disease developed signs of acute intestinal obstruction with abdominal pain, distention and vomiting. He had had an appendectomy two years before. On admission to the St. Louis City Hospital his cardiac condition did not permit more than an enterostomy which was done under local anesthesia without moving the patient from his bed. Part of a tremendously distended loop of small bowel was mobilized, opened and a clamped mushroom catheter inserted inside a purse-string suture which was tied and the wound closed around the tube. The pulse was regular, 100 to the minute. I released the clamp on the tube and 150 c.c. of foul liquid feces escaped under pressure before I replaced the clamp. Immedi-

ately the pulse jumped to 140 and only after ten minutes returned to 100. Sudden drainage was repeated ten minutes later with the same result.

*5. Toxic Symptoms and Death following Rapid Drainage of Obstructed Bowel:*

Case v. N. M. (No. 8177) a twenty-one year old housewife, was admitted April 7, 1929, to St. Louis City Hospital with a three-day history of abdominal pain and vomiting. Her appendix and one ovary had been removed two years before. A diagnosis of intestinal obstruction was made and under nitrous oxide anesthesia supplemented by ethylene I made a right rectus incision. Tremendously dilated small bowel presented in the wound. A glass tube was introduced and between 6 and 8 liters of foul contents removed. It was then easy to find and cut the ileac bands causing the obstruction which were at the site of the previous operation. An enterostomy tube was left at the site of drainage. The operation lasted one hour and at its conclusion the pulse remained under 100 per minute and the respirations and color were good. Seven hours afterward she became restless, then irrational, very noisy and finally had to be restrained. The temperature rose to 102°F. and was recorded as 108°F. just before death, sixteen hours later. A post mortem was not done.

Case vi. J. S. (No. 7073), a twenty-nine year old housewife, was operated on July 23, 1930, for an abdominal mass causing intestinal obstruction of several days' duration. The mass proved to be a twisted ovarian cyst, dark and purplish, which I easily resected. It was then apparent that the pedicle had caused a mechanical obstruction of the terminal ileum. A glass tube was introduced into normal collapsed bowel, through the narrow constricted point, and into the obstructed gut which was dark cyanotic in color but apparently viable. A great many liters of foul liquid feces were evacuated and an enterostomy tube left in at the site of drainage. The operation lasted forty-five minutes, but very soon after she became restless, the pulse bounding and fast, temperature rose to 104°F. and she died four hours later. No autopsy was done.

*6. Toxic Symptoms and Death Developing Spontaneously without Operation:*

Case vii. N. M. (No. 666), a thirty-two year old laborer, was admitted to St. Louis City Hospital after four days of abdominal cramps and vomiting. Five years before he had had an operation for "ulcer and gall-bladder disease." During his stay in the hospital his pulse and temperature varied but were never very high and he had occasional large liquid bowel movements. On the seventh day after admission he became restless and got out of bed. His temperature rose from 98° to 105°F. and his pulse from 100 to 140 within six hours when he died. At autopsy the obstruction was found to be a band causing an almost complete occlusion of the terminal jejunum.

Case viii. A. L. (No. 1808) a forty-nine year old housewife, entered St. Louis City Hospital, May 4, 1929, after six days of abdominal pain and vomiting. Two years before she had a pelvic operation and both tubes and an ovary were removed. *X*-ray showed intestinal patterns, fluid levels, and gaseous distention of a degree diagnostic of intestinal obstruction. Operation was advised but refused. Conservative treatment was given including parenteral saline and gastric lavage and enemata. Her condition seemed good for five days in spite of increasing distention when she suddenly became quite restless and died five hours later. The temperature was not recorded. The blood chlorides before death were normal (670 mg./100 c.c.). No autopsy was done.

*7. Toxic Symptoms and Death in Uncomplicated Deaths from Low Obstruction:* On consulting the records of the fatal cases of uncomplicated low intestinal obstruction in Barnes Hospital I found that most of them died with symptoms similar to those mentioned above, and pointing to the development of a sudden and overwhelming infection, as shown by the frequency of high fever and the presence of symptoms of restlessness and actual delirium before the final coma and collapse. This was true frequently whether or not an operation preceded death. The accompanying table summarizes the data in ten of these cases, and is really self-explanatory.

*8. Collapsed Bowel in Rapidly Fatal Experimental Low Obstruction:* In a series of 16 dogs with a standard low intestinal obstruction I noted at autopsy that 12 of them showed distention; in the remaining

4 the obstructed bowel although then collapsed, had obviously been the site of marked distention at some previous time and one of them showed signs of gangrene. The 12 dogs in which the bowel was found distended at autopsy had lived from five to ten days; the 4 with collapsed bowel two, three, three and four days. This difference was so striking that the inference seemed justified that it was the collapse of the distended bowel which had in some way contributed to the rapid death in these last four dogs. They had not lost a great deal of fluid by vomiting and did not present the anatomical picture of animals which had died of dehydration. These experiments have been described in a previous communication from this laboratory[17] wherein we stated that in these dogs "the bowel was lax and collapsed, but its wall was stretched. Apparently by vomiting and regurgitation the distended loops had emptied themselves. It is of interest that this finding occurred in dogs that died quite soon after the operation."

COMMENT

There can be no disputing the observation, sufficiently attested by the instances just recorded, that successful relief of the occlusion in late low intestinal obstruction may be and is not infrequently followed by serious symptoms and death. That the unfavorable result is directly connected with the coincident release of the intraintestinal pressure seems to be suggested from the evidence described although its proof awaits further data. Certainly the lethal outcome which may occur after surgical deflation of a tense obstructed intestine must either be due to the operation itself (anesthesia, surgical shock) or to some untoward result of the procedure employed during the operation. Against death being due to the operation itself is the fact that immediate recovery is usually good, that many of the patients are young and healthy with a good circulation and normal heart, that the operation itself is usually short, that there is practically no loss of blood and that the anesthesia is sometimes a local one. Moreover, the clinical picture frequently preceding death, i.e. restlessness, delirium, fast bounding pulse, and high fever is not that of surgical shock but rather that of a profound infection. These same symptoms, too, were found in several patients who died spontaneously in whom no operation preceded death. The idea of Wilkie's, already mentioned, that death is a circulatory one due to extensive loss of blood and fluid into the paralyzed dilated splanchnic capillaries is not supported by the clinical symptoms of these patients nor by their failure to respond even when large amounts of blood and fluid are given.

If one assume that the fall of intraintestinal pressure may actually be the cause of death, it is easy to explain the train of events on an entirely mechanical basis. In a distended obstructed bowel circulatory changes in the wall[18] begin very soon and in a few days may become quite marked, and in fact lead to localized patches of gangrene showing through and often involving the muscularis of the wall opposite the mesentery where the circulation is the poorest.

Even in the absence of visible gangrene there is ample evidence of edema, swelling and foci of necrosis and even actual loss of the mucosa in fatal cases examined at autopsy (see Case 11, above, and Table 1). The normal intestinal mucosa, as is well known, is a rather efficient barrier against the entrance of the many poisonous fecal elements which swarm in abundance in perfectly normal lower bowel contents. This barrier depends on the selective action of living intestinal epithelium. When these epithelial cells become necrotic or even damaged this power must certainly be lost or impaired, and as a consequence all sorts of poisons and bacteria may traverse the barrier from the intestinal lumen into the circulation. This idea has been expressed many times in the past[8] but without considering the important element of intraintestinal pressure. It is not the mere

TABLE 1

SUMMARY OF TEN FATAL CASES OF UNCOMPLICATED LOW INTESTINAL OBSTRUCTION

| *History Number* | *Age Sex* | *Duration (Hours)* | *Cause* | *Operation and Anesthesia* | *Death (Hours after Operation or Admission)* | *Symptoms before Death* | *Temperature (C.)* | *Autopsy** |
|---|---|---|---|---|---|---|---|---|
| 24210 | 36 M. | 184(?) | Adhesions—appendectomy 8 yrs. before | Adhesions cut under gas | 10 | Not recorded | ? | (4068) Band occluding midileum. C.P.C. of liver |
| 14216 | 42 F. | 36 | Adhesions—hysterectomy 8 yrs. before | Adhesions cut, enterostomy. Local & gas | 12 | Wild delirium and then shock | 39.3° | None |
| 18071 | 45 M. | 72 | Adhesions of unknown origin | Adhesions cut, enterostomy. Gas & ether | 15 | Shock | 37° | C.P.C. of liver. Many points of obstruction (3596) |
| 6147 | 56 M. | 72 | Adhesions—gastro-enterostomy 3 yrs. before | None | 18 | Wild delirium and then shock | ? | C.P.C. of liver. Band occluding mid-ileum (4054) |
| 19031 | 53 M. | 40 | Adhesions—appendectomy 20 yrs. before | None | 1 | Shock and dyspnea | 41° | Band occluding distal ileum. Mucosa absent above obst. Central necrosis of liver (3961) |
| 7486 | 22 M. | 24 | Adhesions—appendectomy 1 yr. before | Adhesions cut. Ether | 10 | Wild delirium | 40° | None |
| 20709 | 59 M. | 96 | Adhesions—ligation of aorta 3 mo. before | None | 7 | Weakness | 39.6° | Band occluding mid-ileum (2605) |
| 12470 | 39 M. | 72 | Adhesions—appendectomy 4 yrs. before | None | ½ | Stupor | 36° | Band occluding cecum. C.P.C. of liver with central vacuolization (2368) |
| 14835 | 50 F. | 120 | Myomata uteri | Enterostomy. Local (drainage profuse) | 8 | Delirium | 39.5° | Obstruction at terminal ileum by bands. C.P.C. and necrosis of liver (3373) |
| 26647 | 62 F. | 120 | Gallstone | None | 18 | Restless and irrational | 38.5° | Impacted stone at terminal jejunum. C.P.C. of liver (4239) |

* C.P.C. = Chronic passive congestion. Obst. = Obstruction.

presence of damaged mucosa that is important. Every surgeon for example has operated on cases showing foci of necrosis of the dilated bowel wall, cases which previous to operation had nevertheless had no symptoms or signs of "toxemia" (see cases already described). This is probably due to the fact that while intra-intestinal pressure is high enough to interfere with the blood flow through the gut wall an efficient barrier is still present between the fecal content and the circulation; provided, that is, that the pressure is not great enough to force passage through the entire gut wall into the peritoneal cavity. And in spite of certain suggestive observations[8,10,14] most of the evidence thus far is against it.[15,16]

According to this idea, then, the intestinal distention for a time at least acts as a protection against absorption of toxins or bacteria. Now whenever the intra-intestinal pressure falls sufficiently, whether from release of the cause of the obstruction, drainage through an enterostomy or spontaneous emptying due to regurgitation, the blood flow through the gut wall begins again and there is nothing now to prevent intestinal contents from entering the dilated capillaries. It may be that it is not even a question of fecal contents but merely of products of necrotic mucosa already in the intestinal wall, as suggested by Stone.[9] Whether the toxins and bacteria are within the lumen or in the wall, it is obvious that a high intra-intestinal pressure protects the body from their absorption, even though it is the high pressure itself which started the trouble by interfering with the circulation and thus impairing the viability of the mucosal barrier.

One may ask, if these assumptions are true, why it has been so difficult to demonstrate toxins or bacteria in the blood of patients or animals sick or dying of low intestinal obstruction. The attempts to demonstrate poisons in the portal or systemic blood have been numerous and although a few positive results have been reported one must admit that in general the findings have been disappointing.[1] The negative findings, however, are really not surprising and do not necessarily invalidate the theory. In the first place the entrance of bacteria and toxins must be an intermittent affair if it depends on a decrease in intra-intestinal pressure and an increase of blood flow in the walls. There may be no absorption at one moment and a flood of it the next. This conception fits in with the unpredictable behavior of these cases clinically as well as experimentally. If this is true, the blood is probably often collected at the wrong period to demonstrate toxins. This might easily explain the variability in the findings even when positive results are occasionally obtained.[1,19] Secondly, the liver is a great sieve which removes bacteria and toxins more or less effectively so that investigations of systemic blood are especially apt to yield negative results. The finding of changes in the liver, anatomical and functional, by Cole and Elman,[20] even though not uniformly, in dogs with low intestinal obstruction suggests such an action on the part of the liver in protecting the body from harmful elements carried to it from the gut in the portal vein. Similar changes can be noted clinically (see Table 1). It is known, finally, that toxins and bacteria disappear rapidly from the blood and may never be found there even when they are actually responsible for death. Thus Montgomery and Dragstedt[21] have shown that one may kill an animal by intravenous injection of strychnine, for example, and yet fail to demonstrate it in the blood soon after giving it. The same experiment can be done with bacteria. It is also a common experience to get repeatedly negative blood cultures in clear-cut cases of bacterial septicemia.

In view of these intrinsic difficulties we must depend on indirect evidence, of the kind herein described, to show how and why patients die of late low intestinal obstruction. The auto-intoxication theory, while it may be a perfectly valid one, has lacked proof because attention has been

directed to investigations of the nature of the toxin, rather than to the search for the mechanism by which it may reach the circulating blood and the vital centers. There are an abundance of toxic substances and bacteria always available for absorption from both normal and obstructed intestine. The important factor is to determine how they get past the barriers. The element of intra-intestinal pressure in preventing or promoting such a toxemia by its effect on the barriers is one which merits greater study and consideration.

The application of the present evidence to the question of treatment is a vital one, for current practice goes counter to the inferences drawn from the considerations just mentioned. Rapid evacuation of obstructed contents, aided mechanically by evisceration and stripping of the bowel, though generally recommended, is, according to the argument here developed, conducive of a fatal outcome, in certain late cases. That it has been done repeatedly with a satisfactory outcome does not invalidate the argument for it is tremendously difficult to know by inspection of an obstructed gut whether its mucosal barrier is impaired. If the intestinal epithelium still functions it is likely that no sudden lowering of intra-intestinal pressure or mechanical manipulation will alter its protective action. If, on the other hand, the cells have been damaged by the circulatory changes due to the distention, its "vital" function is replaced by purely mechanical laws and sudden lowering of the pressure will permit the return of blood flow and the carrying away of any products in the capillaries of the intestinal wall. When patches of gangrene are visible at operation the change is obvious. But in many cases, this loss of function of the intestinal mucosa is an invisible one, invisible often even on microscopic examination. It explains, however, the greatly variable findings by various observers and serves for the time being at least the useful purpose of making clearer the reason for the lethal outcome in certain cases.

This conception of the cause of death has been recently expressed by Owings and Smith[22] who advocate the actual resection of as much of the obstructed bowel as is non-viable, that is, in the sense of no longer being able to act as a barrier against absorption of toxic elements or as much as is actually necrotic and itself is the source of deleterious substances. They described one case and presented experimental evidence in support of this recommendation but point out the important difficulty in determining at operation how much of the bowel it is necessary to remove. Several patients have recently been subjected to such a procedure with satisfactory results.[23] In a previous communication from this clinic[1] the gradual deflation of the distended bowel was recommended to allow a readjustment in circulation and absorption to take place slowly enough to avoid the deleterious effects which follow sudden changes. A number of patients in which this procedure has been carried out have all recovered.

It is to be hoped that a sufficient number of such cases may be available for adequate study and inference. The important point to be emphasized is the necessity for knowing pathogenesis. When we know the mechanism of the fatal outcome in these neglected cases we may be more hopeful of their satisfactory treatment. The role of intra-intestinal pressure as outlined in this paper would seem to be a promising line of attack both experimentally and clinically.

## SUMMARY

A few clinical and experimental observations have been recorded which suggest that serious symptoms and death may be caused by sudden decrease of the high intra-intestinal pressure present in the distended bowel in certain late cases of low intestinal obstruction. The probable mechanism of this relationship and its obvious application to the treatment of these cases are briefly discussed.

[For References see p. 456.]

# GASTRIC ACIDITY IN CARCINOMA OF THE STOMACH*

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So much has been written concerning gastric acidity in the presence of carcinoma of the stomach, that, at first sight, there would seem to be nothing more to say about it. Closer scrutiny of the literature, however, shows that previous investigators have been handicapped, first, by a lack of standards of normal with which to compare their data from patients, and second, by a cumbersome method of summarizing these data.

Recent work by Vanzant and her associates has now supplied the medical profession with standards of normal for men and women at different ages from youth onward, and also with a method of expressing the mean gastric acidity of any group of patients with a particular disease in simple terms of a deviation from normal. Instead of saying, as of old, that there are certain percentages of persons in the group with anacidity, subacidity, normal acidity, and hyperacidity, we now say that the percentage of persons with anacidity varies by so much from normal, and the mean acidity of those persons with free acid varies plus or minus so many points from the expected normal for a group of persons of the given sex and age distribution.

As a result of these advances in statistical technique, we are now able to detect small differences in acidity such as might be caused by variations in the size or the site of the lesion or by differences in the original secretory activity of individual stomachs.

## TECHNIQUE

The details of the statistical technique will not be given here as they have been described elsewhere. The test meal used consisted of eight arrowroot cookies and 400 c.c. of water, taken in the morning by the fasting subject. A sample was aspirated through a Sawyer tube at the end of one hour. If free acid was present or if there were signs of retention, the stomach was evacuated as completely as possible and a sample from the mixed content was titrated. If no free acid was present and there were no signs of retention, additional specimens were taken at intervals of fifteen minutes for an hour.

If patients did not have free acid after the two-hour test it was assumed that they had true achlorhydria; if acid was absent in the first specimen but appeared during the second hour they were said to have apparent achlorhydria. The terms are used in this sense throughout this report. To simplify the presentation of our results, we are reporting the figures for true achlorhydria. If an additional 4 per cent is added to the figures given for true achlorhydria, the resulting number will represent the percentage of apparent achlorhydria. We do not wish at this time to enter into any controversy as to what might have happened in some of these cases if histamine had been used. We are simply reporting the results obtained with our routine Ewald-type of meal.

*Material.* Material for study consisted of the records of 619 men and 186 women with carcinoma of the stomach seen at The Mayo Clinic, from 1927 to 1931 inclusive. In all these cases, analysis of the gastric content was made and the presence of a carinomatous lesion was confirmed at operation or by the subsequent course of the case.

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*Comparison of Gastric Acidity of Normal Persons and of Persons with Carcinoma of the Stomach* (Fig. 1). Free hydrochloric acid was absent in 62.8 per cent of the men and 55.9 per cent of the women with carcinoma of the stomach. These figures must be compared with the normal of 18.4 per cent for men and 20.3 per cent for women of corresponding ages. In other words, achlorhydria, in patients with carcinoma of the stomach, was approximately three times as common among men, and two and a half times as common among women as it was in our group of normal men and women. Normally there is a greater incidence of achlorhydria among women than among men, but in the case of carcinoma this is reversed because of the curious tendency of carcinoma to depress gastric acidity more among men than among women.

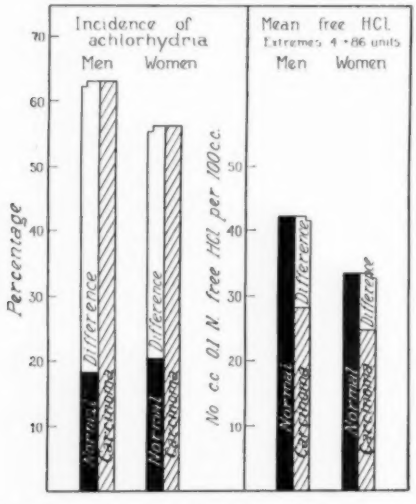


FIG. 1. Incidence of achlorhydria and mean free hydrochloric acid among men and women with carcinoma of stomach and with normal stomachs. Percentages of error for differences from normal are indicated by notching of bar.

After the cases, in which achlorhydria was present, had been analyzed, there were approximately 40 per cent left in which there was free acid, ranging in amount from 4 to 86 units. The mean free acidity was about the same in the two sexes; that is, 28.2 units among men and 24.6 units among women. The deviation from normal was greater among men than among women because the mean acidity of normal men is higher than that of normal women. Actually the downward deviation from normal among the men was 14 units and among the women 8.7 units (Fig. 2). There is not much difference in the acidity in the two groups in the lower part of the range; it is the higher acid values that tend to disappear in the presence of carcinoma of the stomach.

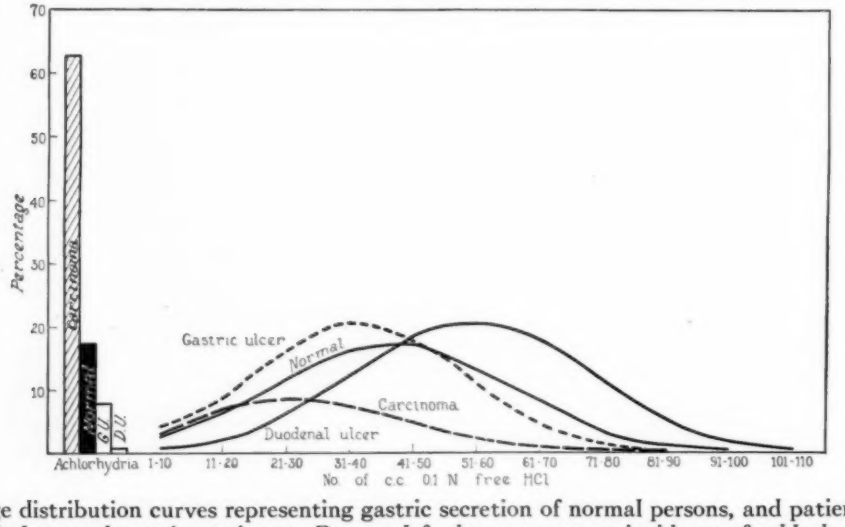


FIG. 2. Percentage distribution curves representing gastric secretion of normal persons, and patients with gastric ulcer, duodenal ulcer, and gastric carcinoma. Bars on left show percentage incidence of achlorhydria in the four groups. In each group sum of percentage represented in bar diagram and percentages delimiting corresponding distribution curve is approximately 96.

*Total Acidity.* In the case of men with carcinoma of the stomach in which free

acid was present, the mean total acidity was 51.5 units, which represents a deviation of approximately 6 units below normal. The mean combined acidity was 23.3, which marks a deviation of approximately 6 units above normal. Among men with carcinoma and achlorhydria, the mean total acidity ranged from 4 to 156 units, with a mean of 19.2 units. This is 3.2 units higher than normal for a group of normal persons with a similar age composition.

### FACTORS INFLUENCING GASTRIC ACIDITY

*Sex.* We have mentioned the decidedly greater depressant influence of carcinoma of the stomach on the gastric acidity of men as compared with its influence on the acidity of women.

*Age.* The mean acidity falls off steadily with age among normal men whereas among women there is practically no fall. Similarly, as shown in Figure 3, with carcinoma of the stomach, the free acidity of men falls off with age, but the rate of this decrease is not as fast as that of normal persons. We were unable to secure definite information on this point concerning women because the number of cases was too small.

Most interesting is the fact, shown in Figure 3, that the steady increase in the incidence of achlorhydria with advancing age is the same among patients with carcinoma as it is among normal persons. The only difference is that the two curves for men and women are moved higher on the chart, owing to the fact that the percentage figures are larger. It is interesting also that in old age there is the same falling off in the percentage of achlorhydria among patients with carcinoma as among normal persons.

*Symptoms.* The material was divided according to symptoms into three groups (Table 1). Group 1 comprised cases in which the symptoms of the patient were those of peptic ulcer, with attacks of hunger pain recurring at intervals over a period of years. This group contained 25 per cent of the men and 23 per cent of the women. Group 2 comprised cases in which the symptoms of the patient were only suggestive of the presence of peptic ulcer. The

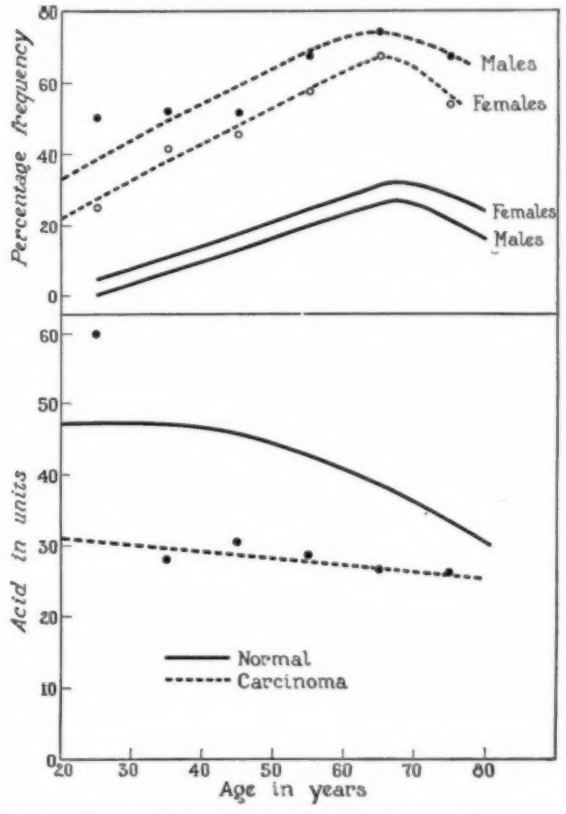


Fig. 3. Regression with age of percentage frequency of achlorhydria among persons with carcinoma of stomach contrasted with that of normal persons (upper). Regression with age of free acid among men with carcinoma of stomach contrasted with that in normal males (lower).

patients all complained of an ulcer-type of distress with relief following ingestion of food and alkalies, but the symptoms were continuous; they lacked the periodicity which one expects in a clear history of ulcer, and there were other details which cast doubt on the diagnosis of ulcer. The duration of symptoms was, on the whole, shorter than in group 1. Eleven per cent of the men and 12 per cent of the women were placed in this group. Group 3 comprised those cases in which the history of the patient did not suggest the presence of an ulcer at any time. In some of these cases, there either was no history of digestive troubles or there was a very short one of vague indigestion which might well have been due to the growth of the carcinoma.

This group included 64 per cent of the men and 65 per cent of the women. For the sake of brevity, groups 1, 2, and 3 will hereafter be referred to as "ulcer-like," "pseudo-ulcer," and "non-ulcer."

Figure 4 shows that in both men and women the incidence of achlorhydria increases as one passes from the ulcer-like through the pseudo-ulcer to the non-ulcer group. The incidence of achlorhydria is practically unchanged in the presence of an ulcer-like history, whereas it is about

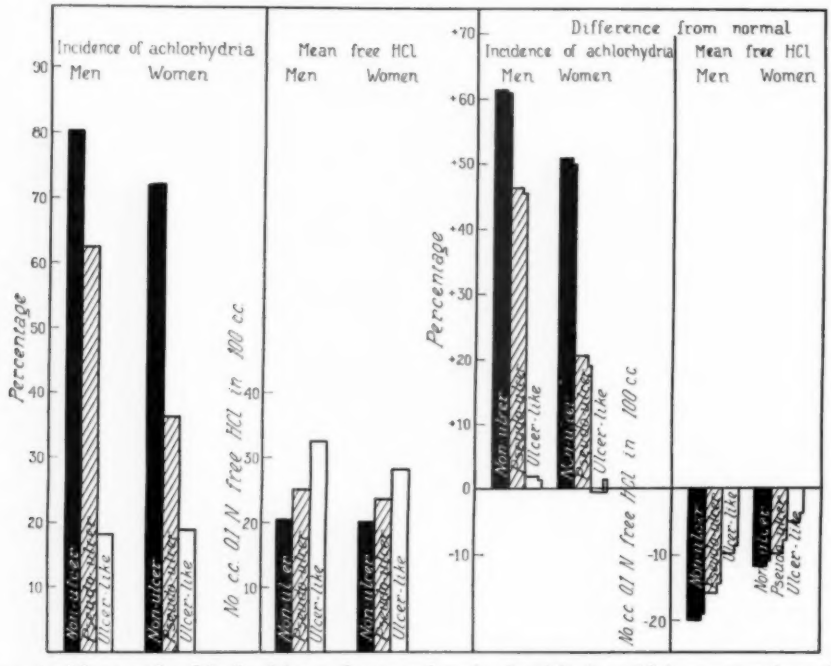


FIG. 4. Percentage incidence of achlorhydria and mean free hydrochloric acid in cases of carcinoma of stomach with ulcer-like, pseudo-ulcer, and non-ulcer symptoms and differences from normal. Percentage of error of differences from normal is indicated by the notching.

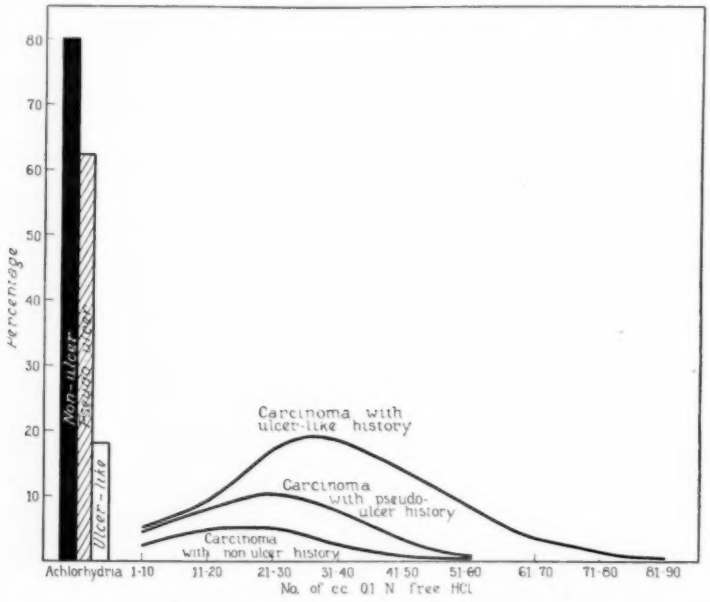


FIG. 5. Percentage distribution curves representing acidity of patients with carcinoma of stomach and three types of symptoms. Bars on left represent percentage incidence of achlorhydria. Sum of percentage represented in bar diagram and percentage delimiting corresponding distribution curve is approximately 96.

four times normal when such history is absent. As one would expect with this, the mean free acidity found in those persons who had free acid falls progressively as one passes from the ulcer-like to the non-ulcer group. The injurious effect of the lesion on acidity was greater in men than in women.

Table 1

| Type of History | Males | | | | Females | | | |
|---|---|---|---|---|---|---|---|---|
| | Number | Per Cent of Total | Age in Years | | Number | Per Cent of Total | Age in Years | |
| | | | Mean | Standard Deviation | | | Mean | Standard Deviation |
| Total..... | 619 | 100.0 | 56.5 | 9.6 | 186 | 100.0 | 55.6 | 11.3 |
| Ulcer-like.... | 156 | 25.2 | 53.6 | 9.6 | 42 | 22.6 | 52.7 | 13.2 |
| Pseudo-ulcer. | 70 | 11.3 | 53.7 | 8.5 | 22 | 11.8 | 49.0 | 11.0 |
| Non-ulcer.... | 393 | 63.5 | 57.8 | 10.0 | 122 | 65.6 | 57.0 | 11.1 |

Figure 5 illustrates the differences in the distribution of gastric acidity in the three groups of patients with carcinoma. All the data are from men, and they have been adjusted to the age of fifty-five years. It will be seen that the range of free acidity in the ulcer-like group was almost normal whereas in the other two groups it was shortened about 40 per cent. In all three groups there was little difference in acidity in the lower ranges up to 20 units. The big difference came after this.

It is evident from Figure 6 that the distribution of gastric acidity in the ulcer-like group was practically the same as that of normal persons or persons with gastric ulcer. Figure 5 suggests to us that some of the cases in the pseudo-ulcer group probably belong in the ulcer group, whereas others belong in the non-ulcer group.

*General Condition of the Patient.* In view of the demonstration by Bloomfield that states of malnutrition and ill health can reduce the level of gastric acidity, we wondered if some of the lowering of acidity seen in cases of carcinoma might be due to the loss of nutrition so commonly seen in this disease. As measures of the general condition of the patient, we had available only notes as to the degree of loss of weight and the presence or absence of anemia. No relation could be demonstrated between the percentage of hemoglobin, on the one hand, and the incidence of achlorhydria and the mean free acid, on the other. Similarly, no correlation was found between the degree of loss of weight and the incidence of achlorhydria and the mean free acidity. It should be noted that at the beginning of our study cases in which the lesion was obviously inoperable were excluded. It was shown by Eusterman and Bueermann that in such cases there is a higher incidence of achlorhydria than in cases in which the lesion is resected or exploration is carried out. It may be that this increased incidence of achlorhydria in the inoperable cases is due, at least in part, to the poorer general condition of

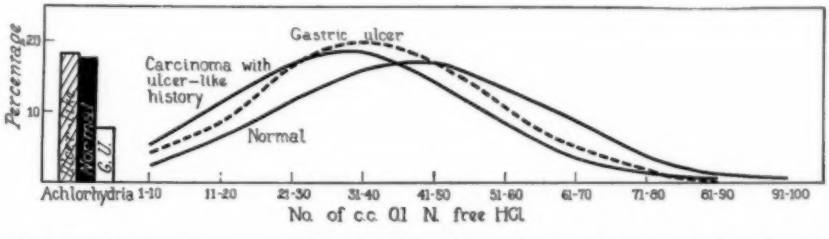


Fig. 6. Percentage distribution curves representing gastric acidity of normal persons, of patients with gastric ulcer, and of patients with gastric carcinoma and ulcer-like symptoms. Bar diagrams represent percentage incidence of achlorhydria in same three groups. In each group sum of percentage represented in bar diagram and percentage delimiting corresponding distribution curve is approximately 96.

these patients, but it may also be ascribed to the greater extent of the disease in the stomach, as will be shown.

*Influence of Duration of Symptoms on Acidity.* Search for signs of such influence served mainly to impress us with the large discrepancy between the duration of symptoms and the extent of the disease. We could find no decided correlation between the duration of symptoms and acidity.

*Influence of the Presence or Absence of a Palpable Tumor on Acidity.* There was a definitely higher incidence of achlorhydria in the cases in which a tumor was palpated. The interpretation of this fact however is difficult because we found in many instances a mass had been palpated before operation although the surgeon found the lesion to be small. Further study showed that retention of gastric contents was generally present in these cases, and it may be that what was felt was a dilated stomach.

*Influence of Volume of Gastric Contents on Free Acidity.* In approximately one-fourth of all cases the volume of gastric content was larger than 250 c.c. In order to determine the effect of the diluting and buffering action of large amounts of retained foods or fluids in cases of obstruction, we studied separately the mean acidity in the total group of cases and the group in which there was no evidence of retention, and strange to say, there was no difference. Furthermore, there was no evidence of correlation between free acidity and volume of gastric content. Apparently the greater stimulus to secretion due to the prolongation of the gastric phase compensates for the diluting and buffering effect of the retained food and liquid.

A well-defined correlation was found between total acidity and volume of contents in the presence of achlorhydria. The coefficient was $+0.493 \pm 0.025$. Although many patients with large amounts of retention were found to have low total acids, a total acidity of 40 units or more was never seen with a volume less than 200 c.c. Combined acidity was also found to be correlated with volume of gastric contents, the coefficient being $+0.310 \pm 0.043$. Combined acidity of 30 units or more usually meant retention of 250 c.c. or more.

*Influence of the Site of the Carcinoma in the Stomach on Secretion.* The incidence of achlorhydria and the value for mean free hydrochloric acid were practically the same no matter where the lesion was situated. In order to rule out a disturbing influence introduced by a possible difference in the sizes of lesions in the upper, middle, and distal thirds of the stomach, we examined the data and found that the ratio between large and small lesions was the same in all parts of the organ. Hartman had previously noted this independence between mean free acidity and achlorhydria and the site of the lesion.

*Influence of the Size of the Carcinoma on Gastric Acidity.* In cases in which the lesion was resected, we had at our disposal measurements made by the pathologist. Figure 7 shows that among men, with all three types of carcinoma taken together, the incidence of achlorhydria increased rapidly with increasing size of the lesion from 17.5 per cent with the smallest carcinomatous lesions to 93 per cent with the largest growths. As one would expect, the mean free hydrochloric acid was also appreciably higher with the smaller lesions. Similar observations were made in the case of women, and then the three types of carcinoma were taken separately. This relationship between size and acidity has been noted previously. Bueermann showed that small carcinomatous ulcers, less than 4 cm. in diameter, were associated with a smaller incidence of achlorhydria than were the larger carcinomatous ulcers.

This increase in the incidence of achlorhydria, together with the decrease in mean free acidity with increasing size of the lesion, would seem to point to a direct depressing effect of the disease on the secretory activity of the stomach. The manner in which this effect is produced is not apparent. The increase in the com-

bined acidity only partially explains the decrease in free acidity. If it were due to destruction of the acid-secreting mucous membrane, one might expect a lower mean acidity with lesions in the upper two-thirds of the stomach, where most of the acid cells are situated, than in the lower third where there are almost no acid cells. Actually, our evidence does not favor the view that destruction of the acid-secreting part of the mucosa is the main factor in depressing the acidity of the gastric juice.

It is possible that the lesion in some way poisons the gastric mucosa, or gastritis, atrophic or infectious, may develop or progress with increased secretion of mucus, and this may not only lessen the secretion but it may increase the neutralization of free hydrochloric acid. Unfortunately we cannot answer these questions until such studies are made of the whole gastric mucosa as will enable us to say just what happens to it in the presence of a carcinoma and just how the changes observed are correlated with gastric acidity.

One of the most interesting results of this study can be seen in Figure 7. There it will be seen that in the non-ulcer group the incidence of achlorhydria with lesions less than 3 cm. in diameter is eight times that observed in the ulcer-like group. Similar differences are found also with larger lesions up to 7 cm. in diameter. With still larger lesions this difference disappears, due probably to the fact that the stomach is about equally destroyed in the two groups. The high incidence of achlorhydria even with the small lesions suggests that in the non-ulcer group the carcinoma often arises in an anacid stomach.

On comparing, in the case of the smallest lesions, mean free acid in the ulcer-like and non-ulcer groups, we did not find any such difference in lesions less than 3 by 3 cm. as we had found in the incidence of achlorhydria. However the probable errors of our figures are large, and it is still possible that with a larger group of cases a definite difference could be shown. From the data now available, it appears that

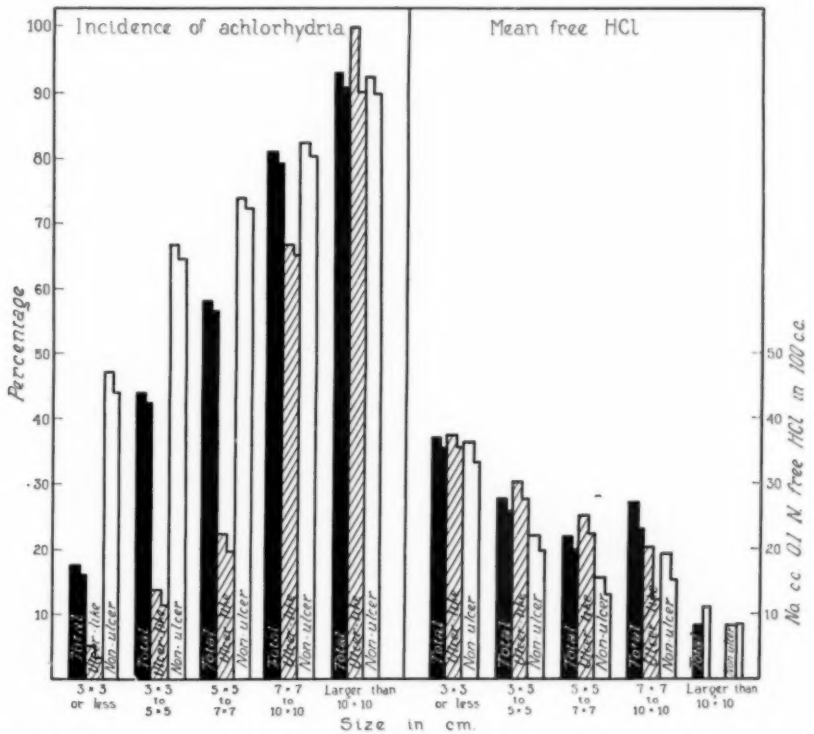


Fig. 7. Influence of size on percentage incidence of achlorhydria and mean free hydrochloric acid in gastric carcinoma. Data for total group of men, as well as for ulcer-like and non-ulcer groups of men are presented. Percentages of error are indicated by notching of each bar.

when carcinoma begins in an acid-secreting stomach, the acidity is not related to the type of symptoms. However, as the lesions grow, those associated with a non-ulcer type of symptoms have a greater depressant effect on the acidity than have those associated with an ulcer-like history.

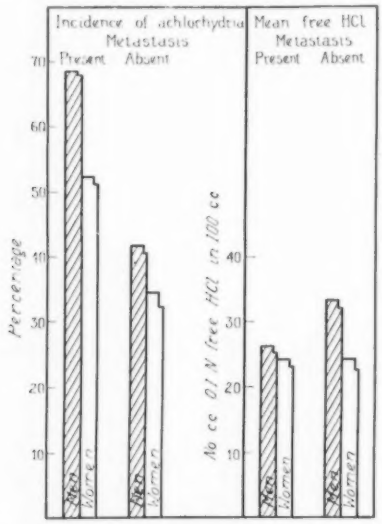


Fig. 8. Incidence of achlorhydria and mean free hydrochloric acid when metastasis is present and when metastasis is absent in both men and women. Percentages of error are indicated by notching of bars.

the presence of metastasis apparently increased the incidence of achlorhydria among men and women, and lowered the mean acidity of men it did not lower the mean acidity of the women (Fig. 8).

*Influence of the Resectability of the Growth on Gastric Acidity.* Our data presented in Figure 9 confirm the observation of Eusterman and Bueermann that the incidence of achlorhydria is greater when lesions cannot be resected than when they can be resected. It shows further that in our material the free acidity was lower when the lesions could not be resected in women but not in men. Separate consideration of the three groups of cases divided according to type of symptoms revealed a greater incidence of achlorhydria in the cases in which the growth could not be resected in both men and women. Similarly, mean free acid was lower in the case of unresectable growths in all the groups except in that of men in the ulcer-like group. It is the high mean acidity in this group which raises mean acidity in the total group of men and explains the difference between them and women. On search-

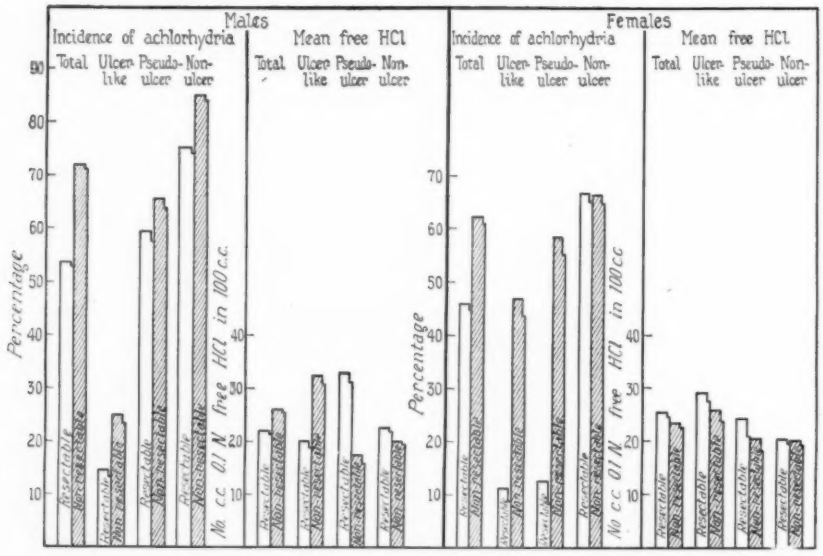


Fig. 9. Influence of resectability on incidence of achlorhydria and mean free acidity in total number of cases and in groups divided according to type of history. Percentages of error are indicated by the notching.

*Influence on Gastric Acidity of Metastasis, Either in Regional Lymph Nodes or in Remote Organs.* It is curious that whereas ing further for a cause of this difference, we found that the presence or absence of metastasis and the site of the lesion in the

stomach played much greater roles in determining the resectability of the lesion then did the size of the lesion. The small size, then, of most of the lesions in this group probably accounts for the high mean acidity. The presence of a comparatively high acidity in the ulcer-like group does not alter the general rule that resectable lesions are associated with a higher acidity and a lower incidence of achlorhydria than are seen with non-resectable lesions.

*Usefulness of Measurements of Gastric Acidity in the Differential Diagnosis between Carcinoma and Ulcer.* Figure 2 shows clearly that there is so much overlapping of the percentage distributions representing free acidity in normal persons and persons with duodenal ulcer, gastric ulcer, and gastric carcinoma that gastric acidity can seldom be of decisive value in making a diagnosis. It must be remembered also that occasionally one sees cases of gastric carcinoma in which there is an even higher concentration of free hydrochloric acid than was encountered in our present series. Occasionally the presence of anacidity, on the one hand, or hyperacidity, on the other, helps in guessing whether a lesion at the pylorus is on the duodenal or the gastric side. Unfortunately, gastric acidity will not help to distinguish a benign from a malignant gastric "ulcer" because the percentage distributions representing acidity in these two types of lesion are so much alike. This point is shown again in Figure 6, and we must conclude that gastric acidity fails the clinician most in just those cases in which he is most desirous of getting help.

## SUMMARY

The records of 619 men and 186 women with carcinoma of the stomach, the nature of whose disease was confirmed at operation or by subsequent observation, and in whom the results of gastric analysis were available, were studied according to a new method. In cases of carcinoma of the stomach the incidence of achlorhydria was about three times the normal and the mean free acidity was lowered about 14 in men and 8 points in women. Curiously, carcinoma seems to injure the acid-secreting mechanism of men more than it injures that of women.

The range of acidity for men with carcinoma of the stomach was from 0 to 90 units, which is only 10 points short of the range for normal men. On comparing percentage distribution curves of acidity of normal persons and of patients with carcinoma of the stomach, one sees that the difference comes in the upper part of the range beyond the point marking 20 units.

In the group of patients with carcinoma of the stomach who had free acid, the total acidity was but slightly lower than normal. In this group the combined free acidity was slightly above normal. In the achlorhydric group, the total acidity was slightly above normal.

The incidence of achlorhydria increased with age among persons with carcinoma of the stomach just as it does among normal persons. The only difference was that the actual percentages at the different ages were greater. Among men with carcinoma of the stomach there was the normal falling-off in free acidity with age, but the curve was different from that of normal men.

Gastric acidity was not markedly influenced by the degree of anemia, loss of weight, situation of the growth, or the volume of gastric contents.

Marked differences in gastric acidity were noted when the cases of carcinoma of the stomach were divided into three groups: according as they had either an ulcer-like, a pseudo-ulcer, or a non-ulcer type of history. In the ulcer-like group the incidence of achlorhydria and the range of free acidity were practically normal and mean free acidity was only 5 or 10 units below normal. The two distribution curves were almost identical. In the non-ulcer group the incidence of achlorhydria was about four times normal. The range of free acidity was shortened by about

40 units, and mean free acidity was lowered by 20 units in the case of men, and by 10 units in the case of women. In the pseudo-ulcer group, the distribution curve representing acidity lay between the other two curves, but somewhat nearer that of the group in which the history was not that of ulcer. The data suggest that in the non-ulcer group, carcinoma often develops in an anacid stomach, and that in the ulcer-like group the lesion begins in a normally acid stomach. The data available do not justify speculation either regarding differences in the disease itself, or as to the probability that carcinoma developed on the basis of ulcer.

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* Continued from p. 446.

# THE ISOIODEIKON LIVER FUNCTION TEST

## AS AN INDEX OF POSTOPERATIVE MORBIDITY IN CHOLECYSTECTOMY*

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THERE are a number of questions concerning the surgical treatment of diseases of the gall bladder which are still unsettled. When these problems are finally solved, it will be as the result of accumulated clinical experience. To add a bit more of clinical evidence on one of these matters, a review of our own small group of recent gall-bladder cases at the Roosevelt Hospital has been undertaken, furnishing the basis of this report.

The question at issue, much discussed of late, concerns the death of patients following simple cholecystectomy from what, for want of a better term, has come to be known as "liver storm."

Heyd[1] in a recent paper has described three types of this clinical condition. In the most common, marked hyperpyrexia and coma develop shortly after operation, death occurring in eighteen to thirty-six hours. The second variety most typically follows operative relief of an obstructive jaundice. Here, a fatal termination results in four or five days in a condition resembling that seen in marked cholemia. In the third type, an anuria begins to develop about forty-eight hours after operation, the urea-nitrogen rises markedly, hyperpyrexia and coma result and death occurs usually from the seventh to the eleventh day.

Whether these three types of postoperative deaths in gall-bladder surgery are varying manifestations of the same condition, or whether they have different causes and different pathology is as yet undetermined. The second type, or cholemic death, occurs in jaundiced cases. Lahey[2] has likened this phenomenon to the disturbance of kidney function which follows relief of urinary obstruction. Clute[3] says: "Sudden relief of common duct obstruction of long duration may be followed by a serious collapse, known as acute liver failure or liver shock. The exact cause of this condition is not known."

The third type mentioned involves, apparently, chemical factors concerned in nitrogen metabolism and is associated with a failure of kidney excretion, due possibly, as Ravdin suggests, to the liberation of depressor substances arising in damaged liver cells. "It is well known," he writes, "that damaged liver tissue contains many such depressor substances."

These two types might seem to be in a measure predictable, or at least susceptible of explanation on the basis of prolonged jaundice with probable liver damage on the one hand, or upon a low kidney efficiency on the other. The first and commonest type, however, occurs in patients who, except for their cholecystitis, appear in all respects to be in good health. The development, following operation, of a rapidly fatal coma with hyperpyrexia in these patients is the clinical picture which we consider most typically that of "liver storm." It is this type which has particularly engaged our attention.

In a previous report from the Roosevelt Hospital Cave[4] found that 10 per cent of all deaths following operations on the biliary tract were due to this cause. In the decade preceding the beginning of this series of cases, from 1922 to 1932, there were 55 deaths following cholecystectomy in the hospital service. Of these 19, or about 34 per cent, were deaths of this type.

* Read before the Section of Surgery, New York Academy of Medicine.

This picture of liver storm following cholecystectomy is unfortunately all too familiar. Following operation, in the typical case, there is likely to be a somewhat unusual rise of temperature, ranging perhaps to 103°F. and suggesting the possibility of atelectasis or pneumonia. Pulmonary signs and *x*-ray findings, however, are negative. The white blood count is not unduly elevated. Nausea and vomiting are likely to be marked. The patient is apathetic and appears sick. In the course of, usually, twenty-four to forty-eight hours, the condition becomes markedly worse. Instead of subsiding, as in the usual postoperative course, the temperature remains high or continues to rise. Vomiting and distention increase and the pulse becomes more rapid and weak. Occasionally, once this critical state is reached, improvement may occur. In most instances, however, the patient continues to lose ground and dies in coma, with a markedly elevated temperature, usually within seventy-two hours, though frequently within forty-eight.

The course and rapidly fatal progress of these conditions suggesting a toxemia rather than an infection, has naturally been ascribed either to some absorption from the liver of the products of damaged tissue or to a failure of the liver, due to trauma or anesthesia, or both, properly to carry on its metabolic functions. Of the two hypotheses the latter has gained the wider credence as a reasonable explanation of the phenomena. It is hardly to be supposed that the small degree of damage to the liver resulting from the necessary handling at operation, nor yet the relatively small trauma to it produced in denuding the gall-bladder bed, should be enough to cause death.

Various tests have been devised for determining the functional capacity of the liver. These functions have been ably summarized by Judd[5] under six headings:

1. Regenerative function. Liver tissue has the power to regenerate after injury.

2. Carbohydrate metabolism: The liver stores glucose as glycogen. It maintains the blood sugar level. (Muscle also possesses these functions in slight degree.) Hypoglycemia and death follow experimental removal of the liver. Tolerance tests with levulose, glucose or galactose are used to determine this function clinically. These tests are not satisfactory as evidences of liver disease because of other factors (activity of the pancreas, for example) which complicate the picture.

3. Protein metabolism: Amino acids, formed from protein by digestion in the intestine, are converted to urea in the liver. This function of de-amidization and urea synthesis is not shared measurably by any other organ. So efficient is the liver in this activity that even a small part of the organ is adequate for carrying it on, as determined experimentally. For this reason there is no satisfactory method of measuring hepatic injury from the standpoint of protein metabolism which might be clinically valuable in surgery.

4. Bile metabolism: The liver secretes the bile acids: glycocholic and taurocholic acids, represented by their salts. They are instrumental in the digestion of fats. Fatty stools show their absence. Bile pigment (bilirubin) is formed in bone marrow and spleen as well as in the liver. The Van den Bergh test provides a means of estimating hepatic injury (principally from obstructive lesions) by determining the amount of this pigment in the circulating blood.

5. Coagulation: The lowering of the fibrinogen level in blood plasma in injury to the liver indicates this organ's importance in the elaboration and control of the coagulating element. Determination of coagulation time is hence a means of measuring liver damage as well as the bleeding risk.

6. Detoxification: The liver is probably active in protecting the body against poisons, toxins and bacteria. It has a large reserve capacity in this function. Hepatitis, which is often found incidentally and without clinical manifestations, may be the result of this detoxifying activity. There is no good means of testing this function

clinically, he concludes. Deaver[6] has particularly noted a relationship between cholecystitis and hepatitis, while Flint[7] in considering this association of the conditions, suggests that the galactose tolerance test is of greater value as an indication of the degree of liver damage present than is the Van den Bergh. If this detoxifying function fails or is suppressed, it is to be supposed that a fatal toxemia might eventually result.

Practically speaking our nearest approach to a clinical method of testing this "cleansing" function of the liver consists in estimating its ability to remove certain substances, artificially introduced, from the blood stream. Following the introduction of the use of the phthalein dyes for radiographic visualization of the gall bladder, it was proposed by Graham[8] that one of these substances might be used for determining liver function as well. Phenoltetraiodophthalein (isoiodeikon) was the chemical proposed. Only the liver will excrete this dye.

Following the intravenous introduction of a solution of 2.5 gm. of the material into the vein, a sample of blood was to be taken a half hour and a second sample an hour later. Incidentally and subsequently the usual *x*-ray pictures were made to determine the visualization of the gall bladder by the dye substance. What percentage of the dye solution should have been taken by the liver from the blood stream (subsequently to be excreted through the biliary system), would represent the liver's functional capacity insofar as concerns its task of removing toxic substances from the blood and its ability to excrete them.

Thus was devised, in this one procedure, a method not only for visualizing the gall bladder but also for testing liver function. This test represented an addition to the previous methods of investigating the liver and was intended to supplement them. The earlier tests, applicable to circulating blood in which abnormal products of liver metabolism were to be sought, depended primarily upon the estimation of biliary substances in it. The Van den Bergh, the icterus index, the cholesterol, the bilirubin tests all would give information concerning the absorption into the blood of biliary materials from the liver, and hence would give some information concerning the bile-producing and bile-secreting activities of that organ. This newer addition to the diagnostic armamentarium would alone give information concerning the one other function of the liver, the excretory, which might supposedly be involved in the production of postoperative liver storm.

It is well known that in the surgery of the gall bladder a high icterus index indicates certain risks in the handling of the case. The same is true of a high degree of cholesterolemia and bilirubinemia. Yet experience has shown that these instances of liver storm may occur in patients who are not jaundiced and whose blood chemical findings are normal, as well as in those showing biliary retention. Some even with much disturbed blood findings fail to develop this complication. Apparently one can not predict the occurrence of this accident solely on the basis of these earlier tests. Likewise, investigation of the blood chemistry before operation of the victims of this accident has shown no consistent or striking abnormality either in the way of a uremia or a hypoglycemia. It has remained therefore a clinical entity, well defined but of uncertain etiology and hence without rational treatment.

Repeated testing with this new method of investigation revealed the fact that, within reasonable limits, once the phenoltetraiodophthalein dye had been introduced into the blood stream all but 15 per cent of it would have been removed at the end of a half hour, and all but 5 per cent at the end of the hour after its introduction. This reading was based on a colorimetric scale.

If, in applying this test in the preoperative investigation of patients suffering from gall-bladder disease, it could be demonstrated that the cases showing higher readings than normal were more likely to

develop liver storm there would then be available a most valuable method for eliminating the graver risks. A patient retaining more than the normal 5 per cent of dye at the end of the first hour after its introduction would then be considered a relatively poor operative risk in respect to the possible development of evidences of liver failure (or liver storm) after operation, even though in all other respects his tests were satisfactory. Conversely, a patient with good dye excretion, within the normal range, would, if the supposition as to its cause were true, fail to develop liver storm even though in other respects his tests were not satisfactory.

To put this theory to further clinical test, a group of our cases, 75 in number, was observed during the past year and a half. These were selected from a total group of 101 cases of biliary tract disease in which operation was performed. To conform to the requirements of this question only those cases were included in which the phenoltetraiodophthalein intravenous dye test was administered, in which simultaneous *x*-ray investigation of the gall bladder was made, and in which cholecystectomy was performed. This eliminated cases of all other types of operation on the biliary tract, as well as all cases which for one reason or another did not receive the dye.

In this connection, it might be of interest to report that it has been contrary to our custom to use the dye in jaundiced cases. There has been a distinct feeling that to administer the dye where some damage to liver cells from biliary stasis has already presumably occurred would but add insult to injury. Moreover, in two or three cases of light jaundice, where the dye was ill-advisedly used, the patients seemed to be made sicker and the jaundice deepened. Also, as Lahey[9] has recommended, the dye has not been used in cases of acute cholecystitis nor in cases of acute cystic duct obstruction with hydrops of the gall bladder. In neither of these groups of cases has the use of dye seemed either necessary for diagnosis or desirable from the point of view of the patient's welfare.

The cases, therefore, which were subjected to this examination were, for the most part, patients suffering from more or less long standing gall-bladder disease. Chronic cholecystitis with cholelithiasis was the predominating diagnosis. This, fortunately for our purpose, includes that group of cases in which liver changes, as a result of protracted gall-bladder and duct disease, are most likely to have occurred, as both Lahey[2] and Eiss[10] have pointed out, and in which, in consequence, the evidence of liver storm (were it due to disturbed liver function) would be most likely to manifest itself.

These patients were prepared for operation in the customary way. Usually it was felt to be desirable markedly to increase the fluid intake for at least twenty-four hours before operation. This was done both by mouth and by vein. In the latter case, at least one infusion of 1000 c.c. of 5 per cent glucose solution was employed. No case was refused operation because of high dye retention readings. In this group were included cases with dye retention as high as 60 per cent after one-half hour and 40 per cent after one hour and as low as 10 per cent after one-half hour and 5 per cent after one hour (Fig. 1).

Gas-oxygen-ether anesthesia was employed in each instance. For this there were two reasons. First, with the methods at our disposal, the use of spinal anesthesia has not given very satisfactory results in operations on the gall bladder. Second, if ether anesthesia were a factor in the production of liver storm, this possible element should not be eliminated in our test.

As to the operations themselves, most of them were done by the writer or by a member of the house staff with the writer's assistance. Thus a similar technique was carried out in almost all of the reported cases of the group. This consisted first in an approach through the rectus muscle or with outward retraction of the muscle

belly from the midline. Exploration of stomach, duodenum, gall bladder, cystic, common and hepatic ducts, and head of denuded gall-bladder bed obstructs the view, and, what is of the greatest importance, any variation or abnormality of

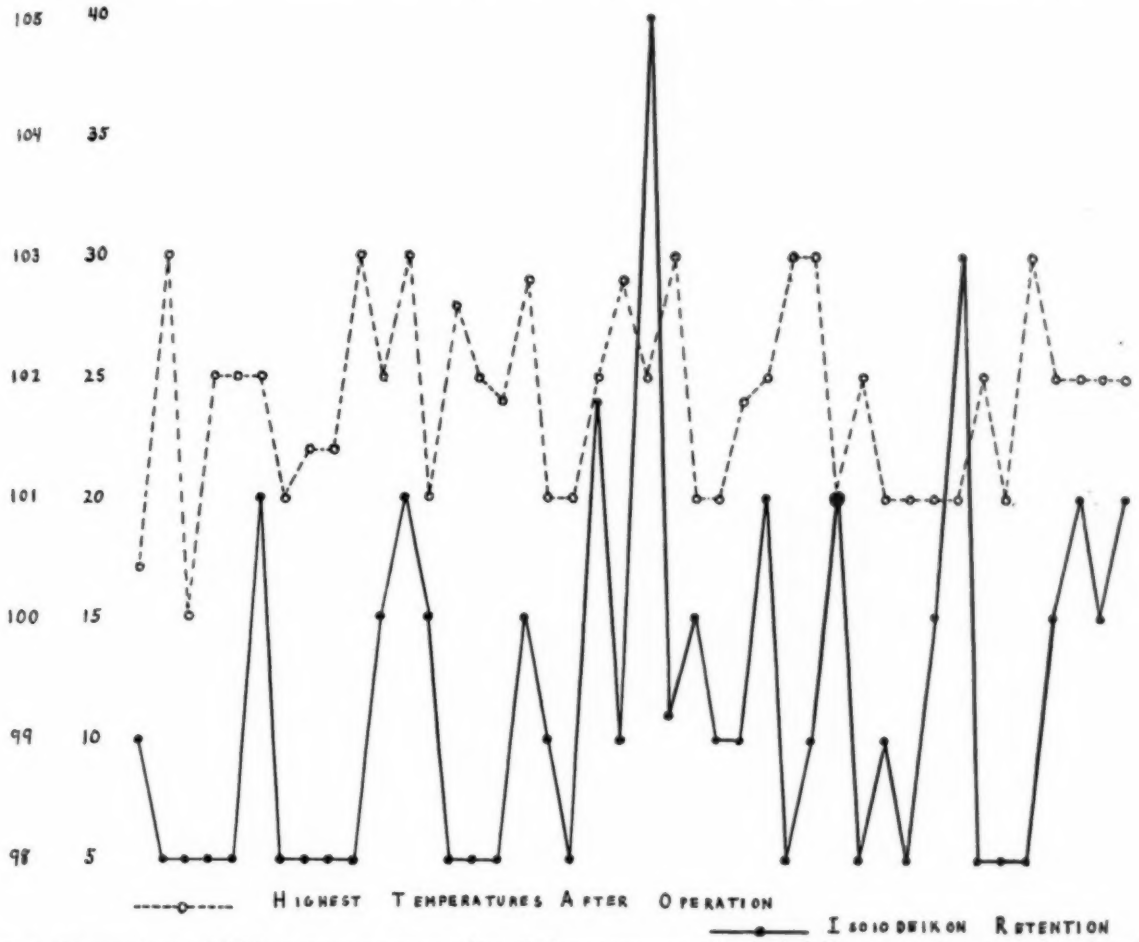


Fig. 1. Comparison of highest temperatures after cholecystectomy with isoiodeikon retention tests (one hour).

pancreas was carried out in each instance, care being observed to traumatize tissue as little as possible. The character of the gross appearance of the liver was also observed. (See Table 1.)

Next, the gall bladder was removed. In all but three instances this was done from the cystic duct toward the fundus. It seems well here to express a distinct personal preference for this type of operation. First one attacks the major problem of the isolation and ligation and division of the cystic duct and artery while anatomical relations are as yet undisturbed, and in a clean and dry operative field. The structures, in their normal relations, may readily be identified. No oozing from a the arrangement of important structures (notably of the hepatic artery) may be observed and provided for. There is also no undue traction upon or angulation of the common duct, such as may so easily occur when a detached gall bladder is used as a tractor to facilitate the clamping, ligation and severance of the cystic artery and duct, a practice which more than once has led to unanticipated and unrecognized injury to the common duct.

This practice of removing the gall bladder from the duct outward was found rarely to involve much difficulty. Even in those cases where the presence of old adhesions or an enlarged or distended gall bladder, or abnormal amounts of fat in the

abdominal wall and about the viscera threatened unusual technical obstacles, it was still usually possible to perform the operation in this way. It is the writer's feeling that particularly in these more difficult cases it is important first carefully to identify the important structures before attempting removal of the gall bladder, for it is in these cases that injury is most likely to be done. In the 1922–32 group, previously mentioned, 15 of the 19 patients who died in a condition resembling liver shock had the gall bladder removed from the fundus inward.

TABLE 1

| *Duration of Symptoms* | *Dye Retention (Per Cent)* | *Icterus Index* | *Highest Temp. Postop.* | *Condition of Liver* |
|---|---|---|---|---|
| 3 yr. | 20 | 43.2 | 103.5 | Moderate cirrhosis |
| 2 wk. | 15 | 25.2 | 101.2 | Normal |
| 1½ yr. | 5 | 13.5 | 101. | Slight cirrhosis |
| 3 d. | 10 | 27.4 | 103.8 | Slight fibrosis |
| 4 yr. | 5 | 6 | 101.2 | Normal |
| 1½ yr. | 10 | 14. | 103.8 | Normal |
| 4 d. | 5 | 12. | 102.2 | Normal |
| 1 yr. | 5 | 10.7 | 102. | Slight fibrosis |
| 3 yr. | 10 | 7. | 102.4 | Slight fibrosis |
| 2 yr. | 15 | 4. | 103.5 | Normal |
| 2 yr. | 20 | 12.8 | 102. | Moderate fibrosis |
| 2 yr. | 15 | 12.15 | 102. | Normal |
| 3 yr. | 10 | 31. | 103. | Normal |
| 2 yr. | 17 | 25. | 103. | Slight fibrosis |
| 11 yr. | 25 | 12.7 | 101. | Moderate fibrosis |
| 6 mo. | 10 | 12.9 | 101.2 | Normal |
| 3 yr. | 5 | 7.9 | 101.2 | Normal |
| 4 yr. | 40 | 8.8 | 102.2 | Moderate fibrosis |
| 3 yr. | 10 | 7. | 101. | Slight fibrosis |
| 2 yr. | 10 | 5.1 | 101.8 | Normal |
| 8 yr. | 20 | 5. | 101. | Moderate cirrhosis |
| 4 yr. | 5 | 6. | 102. | Normal |
| 5 d. | 10 | 10. | 100.5 | Normal |
| 3 mo. | 5 | 12. | 102.2 | Normal |
| 7 mo. | 10 | 32. | 102. | Normal |
| 3 yr. | 5 | 6.7 | 103.5 | Normal |
| 2 yr. | 15 | 12.1 | 102.2 | Normal |
| 1 wk. | 5 | 9.1 | 102.8 | Normal |
| 3 yr. | 15 | 12.1 | 101.2 | Slight fibrosis |

The following cases are not included in the group of cholecystectomies. They received only palliative operations, as demanded by the clinical condition.

| *Duration of Symptoms* | *Dye Retention (Per Cent)* | *Icterus Index* | *Highest Temp. Postop.* | *Condition of Liver, Etc.* |
|---|---|---|---|---|
| 8 mo. | 40 | 104. | 104.5 | Diffuse metastases, Ca. |
| 6 d. | 80 | 120. | 102. | Acute hepatitis |
| 1 mo. | 30 | 17.1 | 101. | Slight fibrosis |
| 5 wk. | 15 | 33.5 | 102. | Moderate cirrhosis |
| 1 yr. | 12 | 13.6 | 103.2 | Normal (Suppurative g.b.) |
| 10 yr. | 15 | 8.9 | ..... | No op. Marked cirrhosis |
| 2 yr. | 5 | 70. | 101. | Marked cirrhosis |

Two cases in the present series rather clearly illustrated one of the hazards to be encountered. There was found an abnormally placed hepatic artery in each paralleling and closely adherent to a tortuous cystic duct. The artery would almost certainly have been injured had the cholecystectomy been begun at the fundus.

Careful retraction and padding off of neighboring viscera has been found of the first importance. In the more recent cases, it has been our custom, when the gall bladder is much distended, to empty it with trocar and cannula (subsequently clamping the opening made for this purpose) before attempting identification of the duct and artery. This plan has two advantages. It removes a considerable obscuring bulk from the operative field, thus facilitating the work. In the second place it avoids the expression of possible septic material into the hepatic ducts and their tributaries by manipulation of the distended sac, an accident which may well predispose to a cholangitis.

Following division of the cystic duct and artery the gall bladder was, in the cases of this group, removed from its bed in the liver with as little damage as possible to liver tissue. The serosal coat was left intact wherever possible. Damage to liver was thus largely avoided and oozing minimized. In only two instances was it necessary to introduce hemostatic mattress sutures in the edges of the liver bed. In all of the others no attempts at closure were made. In each instance the field was left dry. Before closure of the wound a rubber drainage tube was always introduced to Morison's pouch, led out either through the rectus muscle or through a lateral subcostal stab wound. This drain, designed to care for serous ooze or for accidental biliary spilling, was left in place for but forty-eight hours and then withdrawn.

The technical steps of the operation have been thus rather fully outlined because of the conclusions which were drawn from this group of cases.

Following operation the care of the patients followed a rather set schedule. Fluids were administered liberally by vein, rectum and clysis. Morphine was used to control pain during the first two days. Fluids by mouth were begun as soon as vomiting was controlled, giving place to soft diet usually on the third day. This, in turn, was replaced by a rather liberal low-fat diet about the fourth day. Patients were allowed out of bed on the twelfth to the fourteenth day.

As in any operative series, this group was not without its complications. There was one death in the series, from pneumonia. (See Table II.)

TABLE II
COMPLICATIONS

| *Name* | *Highest Postop. Temp.* | *Nature of Complication* | *Dye Retention (Per Cent)* |
|---|---|---|---|
| W. | 103.5 | Excessive vomiting | 10 |
| U. | 103.8 | Prolonged drainage | 10 |
| C. | 103.5 | Continued fever to 20 d. | 20 |
| B. | 105. | Atelectasis R.U. lobe | 5 |
| E. | 103. | Continued fever 10 d. | 10 |
| S. | 105.2 | Pneumonia | 5 |
| B. | 103. | Fever 38 d. Ca. of G.B. | 5 |
| S. | 104. | Pneumonia. Died 6 d. | 20 |
| Z. | 102. | Atelectasis R.L. lobe | 5 |
| B. | 101. | Bronchitis | 5 |

Among the postoperative complications, however, there was not a single case of liver storm. As far as could be observed there was no higher incidence of postoperative morbidity in those cases showing a high dye retention (and hence, presumably, diminished liver function) than in those which showed normal readings by this dye test. The temperature of these patients ranged, on the average, no higher, returned as rapidly to normal and their recoveries were as generally uneventful as were those of their fellow patients. Their convalescence was not unduly retarded and their subsequent recovery, as determined by follow-up examinations, was not delayed.

It had been the original intention to pursue this investigation over a greater period of time and to cover a much larger group. It was found that the administration of the isoiodeikon was productive of a large percentage of untoward reactions. Fully 35 per cent of the patients receiving it developed a marked urticaria, vomiting or fever, or all three of them. In the medical service of the hospital, where iodeikon (tetraiodophenolphthalein) was used for gall-bladder visualization it was noted that these reactions were much less common, while the method of administration was the same and the results, as far as radiographic investigation was concerned, fully as satisfactory. The use of the phenoltetraiodophthalein was therefore discontinued.

It cannot, of course, be considered as proved, on the basis of this investigation, that there is no definite relationship between dye retention (as thus estimated and as indicative of impaired liver function) and the postoperative development of liver storm, especially in view of the absence of an instance of this accident in our series. Graham's[8] recent report, describing a reduction in mortality of patients operated upon for biliary tract disease, is impressive. In comparing two three-year periods—one before, the other after employing isoiodeikon for the discovery of bad surgical risks, there was a reduction of deaths in his cases from 6.5 to .5 per cent. Such results as he cites cannot be ignored. The value of the method as an adjunct to the other available tests for estimating liver function is clearly indicated. Yet of itself, in our experience, this test may supplement but cannot altogether supersede our other means of investigation to determine the patient's ability to withstand operation. There are, we believe, other factors not only in the patient's general condition, but even in relation to the liver itself which should have as much if not more weight in influencing the surgeon's decision.

In our own brief series, in which the isoiodeikon test was not relied upon as a

criterion of operability, the mortality was a little more than 1 per cent (1 in 75).

It appears that the phenoltetraiodophthalein test is reasonably confirmatory of the other tests of liver function. In the cases in our group giving the highest dye retention readings the icterus index and bilirubin tests often showed distinct evidence of liver damage (see Table 1). Two cases not included in the group with retentions over 40 per cent at the end of an hour, and one with 80 per cent, showed also abundant clinical evidence of the severity of their illness and on that account were not subject to cholecystectomy. One of these had a carcinoma of the pancreas with a liver riddled with metastases, while two others had advanced cirrhosis and received only palliative operations. On the other hand one patient with a retention of 40 per cent, but without other evidence of serious illness or liver insufficiency, supported a cholecystectomy without any untoward results.

In the appended chart (Fig. 1) is shown how a comparison was made between the dye retention readings in this group of cases and the postoperative temperatures. This is not as unfair a comparison as might at first appear, as those cases which showed any complication that might account for the elevation of temperature have been excluded, and the operations of cholecystectomy were all done in the afebrile stage. Hyperpyrexia being the most consistent feature in liver storm, it was felt that this might serve as a crude measure of postoperative morbidity. A glance at the chart will show that there is no apparent parallel between the amount of temperature elevation and the degree of dye retention.

The suggestion seems quite clearly indicated that in the negative sense at least, in the absence of other clinical and laboratory evidence of impending danger, we cannot look to this test alone with any degree of assurance as a means of predicting the occurrence of liver storm. We must therefore seek elsewhere for an explanation of this dreaded accident and for some other means of anticipating it.

It is distinctly the impression of the writer that the explanation may well rest in the field of surgical trauma. For instance injury to or ligation of the hepatic artery or any of its hepatic branches would produce necessarily profound effects, first in the death and consequent loss of function of liver tissue, and second in the absorption of degeneration products of the tissue destroyed. That such an accident might easily have fatal consequences may readily be imagined. In fact, Graham[11] has collected 28 instances of this accident with 15 deaths. In the fatal cases cited in his report the patients developed, following operation, hyperpyrexia and evidence of liver function failure. Increased amino-acids appeared in the urine and a hypoglycemia was occasionally present. Most of the deaths occurred in thirty-six to seventy-two hours, though the interval in which death occurred extended from three hours to twenty days. Greater or less degrees of liver necrosis were found at autopsy. He suggests that the patients who did not succumb were saved by a collateral circulation through the diaphragm sufficient to prevent too extensive a necrosis of liver substance.

That old age, impaired heart and arteries, cirrhosis, hepatitis, impending uremia, diabetes and marked jaundice constitute hazards in the path of a patient subjected to operations on the biliary tract there can be no doubt. That acute infection in the gall bladder or bile passages represents a very special danger to the patient faced with operation is now accepted by some. But the usual morbidity and mortality resulting from these risks, distinct from the liver storm, are more or less to be predicted and do not lack explanation.

Until further experience or investigation shall definitely establish the cause of liver storm in patients who are not subjected to these special risks, we must continue to feel that its production or its avoidance may well rest in the hands of the operator. The

best means of preventing it would seem to be the elimination of poor risks on both clinical and laboratory evidence, the careful observance of technical accuracy at operation and the strict avoidance of injury to the hepatic artery, to the liver and to the common duct.

## SUMMARY

1. The isoiodeikon liver function test, as an index of postoperative morbidity in operations on the biliary tract, has been observed in a group of 75 cases of cholecystectomy.

2. No constant relation has been discovered between the findings of this test and the postoperative course in the cases observed.

3. The test corresponds roughly to the icterus index findings and to the observed condition of the liver at operation, particularly where the variations from normal are marked.

4. It is suggested that postoperative deaths from liver storm in some cases, where the various tests do not suggest greatly impaired liver function, may be due to other factors; possibly to surgical trauma.

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* Continued from p. 437.

# UNUSUAL COMPLICATION WITH A LEVINE TUBE

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WINNETKA, ILL.

NOW that the use of the Levine tube is rightfully becoming more popular, one has to be watchful of any potential complications that may arise either directly or indirectly from its use. So far as I have been able to learn, the embarrassment of having a knot become tied in the end of the tube by the peristaltic action of the stomach has been unknown.

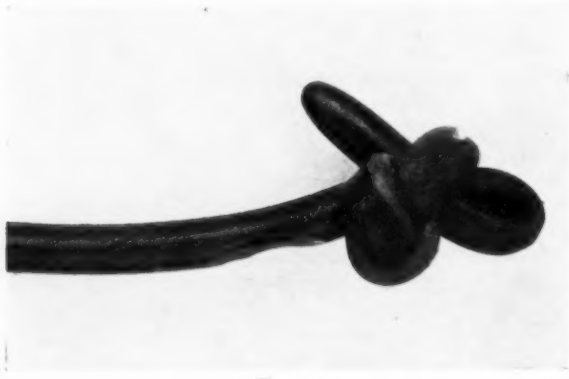

FIG. 1.

In the case under question, the patient had a Levine tube passed through her left nostril immediately after a cholecystectomy. The tube was aspirated every half hour for the first forty-eight hours, during which time the patient was very comfortable. At the end of forty-eight hours, the nurse found that the tube apparently had become clogged. The tube was then withdrawn, but great difficulties arose in bringing the distal end out through the nostril. When it was finally out. a double loop knot, measuring 1.7 cm. by 2.6 cm., as shown in the photograph, was seen.

I believe two factors predisposed the knot formation: in the first place, the tube was old, very soft, and pliable; secondly, extra holes had been cut into the tube so as to provide drainage from both the stomach and duodenum should the end of the tube pass through the pylorus. These extra holes, of course, added further pliability to the tube.

Fortunately in this instance no serious difficulty arose. I believe, however, that the potentialities may be greater. I further believe that old, soft tubes should be discarded and only newer stiffer ones used. By so doing, there will be much less chance of the peristaltic action of the stomach producing such a condition.

# SUBPHRENIC (SUBDIAPHRAGMATIC) ABSCESS*

LEON M. BOGART, M.D.

FLINT, MICH.

BARLOW[1] described a subphrenic abscess in 1845 and Volkman operated upon a case in 1870. Barnard,[2] to whom credit is due for the masterly presentation of the subject in 1908, defines a subphrenic abscess as a collection of pus in contact with the under surface of the diaphragm. He also thought that an abscess of the liver close to the surface belongs in the same class.

## ANATOMY

Barnard[2] divided the subphrenic space into six anatomic regions: anterior right and left intraperitoneal, posterior right and left intraperitoneal and right and left extraperitoneal (Fig. 1.)

## ETIOLOGICAL FACTORS

Infections in the vast majority of the cases, secondary to intra-abdominal lesions though cases of unknown origin occur, and have been reported (see Case II). In 1000 collected cases Whipple[4] found 25 per cent followed lesions of the stomach, 21 per cent appendix, 16 per cent biliary, 5 per cent duodenum. The remainder were accounted for by lesions of almost any other abdominal organ.

Empyema seldom, if ever, causes subphrenic abscess. Schwartz,[5] in 150 cases of empyema, never encountered a single case, though Bye,[6] in 190 cases of empyema thought that one case of subphrenic abscess resulted from trauma during operative procedure. The infection may travel upwards from the appendix, via the right paracolic groove (Fig. 2) into the right anterior or posterior intraperitoneal spaces, and extend into the lesser peritoneal cavity (left posterior peritoneal space). Infections from the pelvis may travel upwards by the left paracolic groove and localize in the left intraperitoneal spaces. Clark[7] reported a case following a criminal abortion, in which the autopsy revealed a left subdiaphragmatic abscess with a perforation of the left pleura. Clark also reported a right subphrenic abscess following a hysterectomy and right salpingo-oophorectomy. Dexter[8] pointed out that the lymphatics of the subphrenic spaces are in communication with the abdominal cavity, through the retroperitoneal cellular tissue, through the lymphatics of the appendix and colon to the falciform ligament and finally through the lymphatics of the diaphragm to the pleural cavities. Echinococcus cyst of the liver may be of etiological significance (Case VII).

The pathology is that of a localizing abscess, in many cases complicated by gas formation due to colon bacillus. Localization may occur in any of the spaces as outlined by Barnard. The right side is the most common and follows appendicitis, duodenal and gastric perforated ulcers. The left side will be involved most commonly in perforations of the lesser curvature and cardio-esophageal angle. The left anterior and posterior intraperitoneal spaces may also be involved, following ruptures of gastric or duodenal ulcers. Following gall-bladder involvement, the right posterior intraperitoneal is the space most commonly affected. Although the diaphragm is an excellent barrier between the abdominal and pleural cavities, extension may take place by lymphatics or solution of continuity. Long[10] states that from 25 to 35 per cent of subphrenic abscess will eventually perforate into the pleural cavity.

* Presented before a Sunday conference of the Hurley Hospital staff.

As previously pointed out, the anatomical spaces intercommunicate and involvement may be in more than one space. Most of the cases reported are acute and follow within three weeks of the primary cause. Gatewood[11] reported a case of seven years' duration between primary and secondary operation.

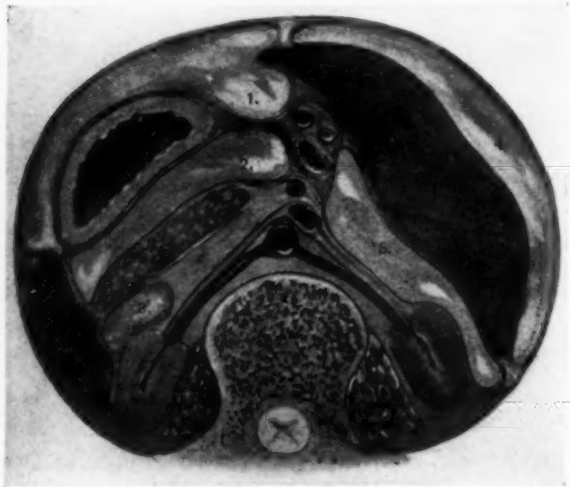

Fig. 1. (1) Left anterior intraperitoneal space, formed by stomach and spleen, left lateral ligament and diaphragm above, floor formed by the tail of the pancreas and left kidney. Abscess in this region is usually due to a ruptured gastric or duodenal ulcer. Best drained by anterior abdominal approach.

(2) Left posterior intraperitoneal space, corresponding to lesser peritoneal cavity, communicating with the right posterior intraperitoneal space (5) through the foramen of Winslow. Abscess in either right or left intraperitoneal spaces may spread readily into each other. Ruptured gastric or duodenal ulcers commonly are etiological factors, though cholecystic disease has been reported as primary cause. Anterior abdominal approach is perhaps least difficult in securing drainage.

(3) Left extraperitoneal, above upper pole of left kidney. Perforation or cancer of esophagus, pelvic lesions or perinephritic inflammatory processes are usually responsible. Best approach is usually transpleural or the Nather and Ochsner method, described under treatment.

(4) Right anterior intraperitoneal, diaphragm, anterosuperior surfaces of liver bordered by right lateral and falciform ligaments, communicating with right posterior intraperitoneal space (5) and right pericolic groove (Fig. 2). Infections around cecum and right pelvis may easily cause pus accumulation in this space, one of most common locations. Ruptured appendix or gastric ulcer most common etiology. Surgical approach depends on extent of involvement. If posterior, right intra-abdominal space is also involved, retroperitoneal approach according to Nather and Ochsner[3] is best. Older authors feel that subcostal anterior abdominal incision is conducive of better results.

(5) Right posterior intraperitoneal space is formed in front by liver and gall bladder, laterally by abdominal wall and posteriorly by crux of diaphragm and upper pole of kidney. It connects with lesser peritoneal space (No. 2, left intraperitoneal space) through foramen of Winslow. Majority of subphrenic abscesses are formed here. Ruptured appendices, gastric ulcers and acute suppurations of gallbladder are often etiological factors. Best surgical approaches, subpleural, dissecting reflection of pleura or transpleural suturing pleura to diaphragm and drainage or subdiaphragmatic space between sutured layers of pleura. Posteriorlumbar route of Nather and Ochsner[3] has given excellent results and appears to be less shocking. (After Fifield and Love.[16])

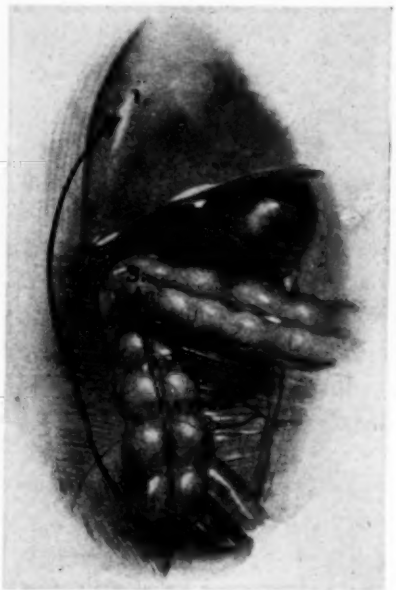

Fig. 2. (1, 2) Right anterior and posterior intraperitoneal spaces, showing mode of infection along paracolic groove, following infections in region of cecum, the two most common sites.

(3) Right extraperitoneal, the area enclosed by folds of the coronary ligaments. Infections travel upwards from region of appendix (especially retrocecal) along the extraperitoneal cellular fissure, the third most common space affected following appendiceal infections.

Surgical approach, subpleural or transpleural, or posterior lumbar approach of Nather and Ochsner.[3] Space marked 3 on Figure is the 6th space mentioned by Barnard. (After Fifield and Love.[16])

The symptoms are rather vague, suggesting the presence of pus and infection in the gall-bladder area. Continued temperature and chills, hiccough, unproductive cough, subcostal tenderness which persists, or sometimes the pain is in the epigastric region. Often the pain is referred to the neck. The white blood count is high and in cases of prolonged standing, secondary

anemic changes are present. Russell[12] reported 3 cases in which subphrenic suppuration was found seven months, one year and seven years following the primary cause.

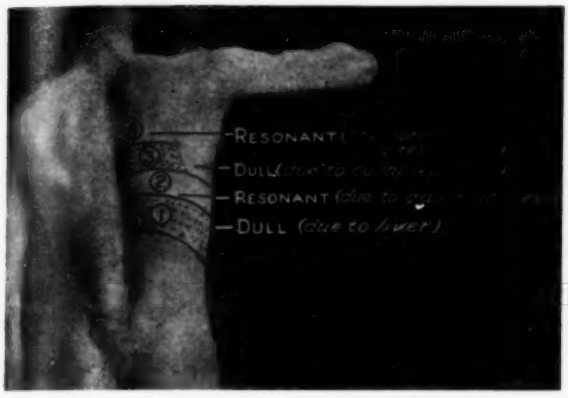


Fig. 3. Signs that may be present in a fully developed subdiaphragmatic abscess with gas formation. (After Bailey; Physical Signs in Clinical Surgery. Wm. Wood & Co.)

The physical signs are of great importance if properly interpreted. A large percentage of subphrenic abscesses will show early signs referable to the pleura and lungs. Retarded costal excursions on the affected side and even acute scoliosis has been noted, due to spasm and contracture of the quadratus lumborum. Percussion may reveal areas of altered resonance (Fig. 3).

The liver may become firmly adherent to the costal arch and the lower area of dullness may not change, the abscess pushing upwards. An increased flare in the costal margin may be present.

X-ray findings are of utmost importance, although they may appear somewhat late and when present are the determining factor in immediate surgical release of the accumulated pus. Elevation of the diaphragm on the affected side occurs, the arch becoming more acute than normal. If gas is present in the abscess, then the characteristic gas bubble will become evident, otherwise the homogenous appearance of the mass below the diaphragm will blend with the liver area and will show an increase in the normal vertical liver density. The costophrenic angle becomes obliterated, due to a pleuritis. Anteroposterior and lateral views should be taken; the anteroposterior view determines the side

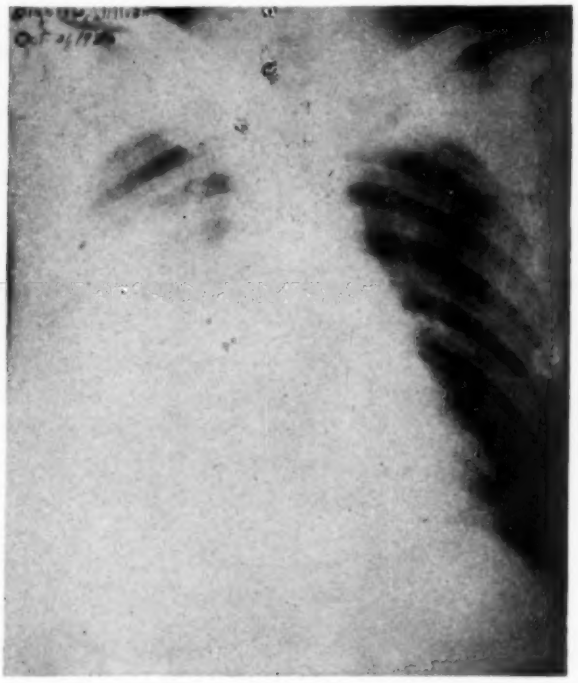

Fig. 4. Case III. Massive diffuse homogenous shadow on right side, obliterating the lower costal marking, as well as the diaphragm. Case proved to be a perforated subphrenic abscess, communicating with branch of main bronchus; terminated fatally.

affected, and the lateral may be of value in locating the space involved. Fluoroscopy is of use in visualizing the movements of the diaphragm, as well as the form the diaphragm assumed. Dexter[8] noted on fluoroscopic examination in a left-sided subphrenic abscess the agitation of the fluid by the heart beat.

Subphrenic abscess must be differentiated from neoplasms of the liver, perinephritic, intrahepatic abscesses and empyema. The history, the blood count and signs of sepsis should lead one to differentiate a suppurative process from a neoplasm.

Empyema will be differentiated by the physical signs and *x*-ray findings. In empyema the fluid level is s shaped, while the subphrenic abscess is dome-shaped as determined by the shape of the diaphragm. The heart is rarely, if ever, displaced in subphrenic abscess, usually displaced in

empyema. The diaphragm is almost immobile or dome-shaped in subphrenic abscess. If the lungs and pleura have become involved, it may be impossible to distinguish the true condition. Insertion of a trocar is usually considered to be fraught with danger, unless one is prepared to operate immediately following puncture.

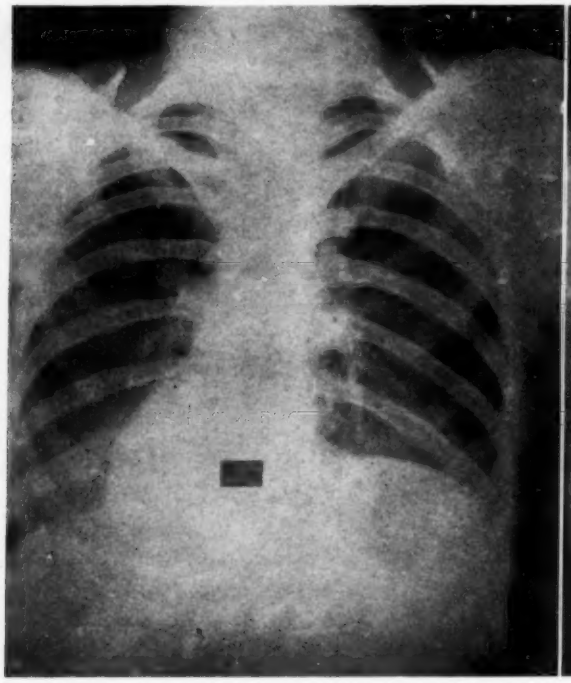

Fig. 5. Case iv. Taken January 2, 1931. High right diaphragm and full arch. Compare with Figure 6, taken June 8, 1933, showing normal dome of right diaphragm.

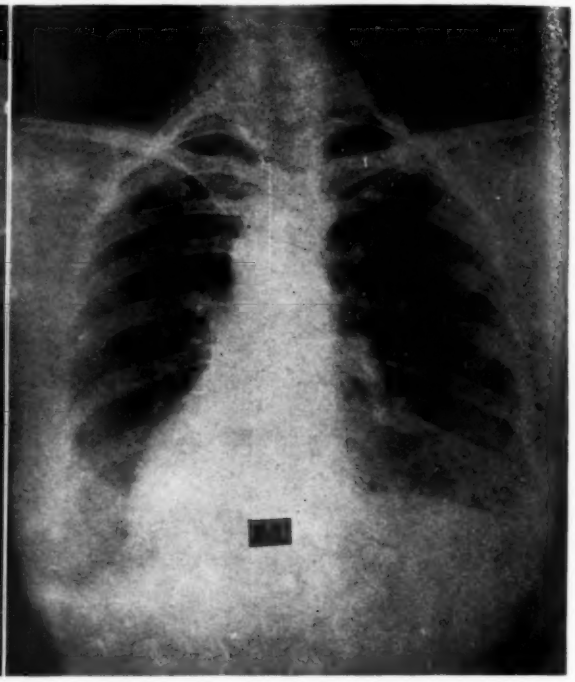

Fig. 6. Case iv. Re-ray of Case iv, two and one half years following successful drainage of a subphrenic abscess; arch less apparent. Compare with Figure 5.

The course of subphrenic abscess may be acute or insidious and unless treated by proper drainage it is usually fatal. Mortality and morbidity are in direct proportion to early diagnosis. Lockwood, in 81 cases in which operation was performed, had 27 deaths (33 per cent); in 32 cases in which operation was not performed he had 31 deaths (99 per cent). Gatewood[2] operated on 38 patients, with 11 deaths (29 per cent); in 3 cases in which operation was not performed he had 3 deaths (100 per cent). Elsberg[14] in 1901 reported a mortality of 82 per cent in cases with no operation.

## TREATMENT

*Prophylaxis* comprises allowing gravity drainage by institution of the Fowler position in all suppurative processes in the abdomen as soon as possible. When the patient lies in the straight horizontal position, the lumbar region is the highest point of the posterior abdominal cavity, and determines to a great extent the accumulation of the septic fluid. In active treatment, the difficulty of proper drainage is due to: (a) the long course of the drainage tract, whether it is drained from above or beneath the liver; (b) the low pressure of the upper abdomen retarding drainage and favoring collections in pools, and (c) the change in the costal arch and diaphragm during respiratory excursions which lessens the pressure on the walls of the abscess cavity. In the lower abdomen an abscess cavity tends to obliteration, aided by gravity and of the structures, while the infected spaces between the diaphragm and the liver are not obliterated readily, due to the causes already stated.

The *surgical approach* of a subphrenic abscess depends a great deal upon the space involved: (a) the abdominal route; (b) the thoracic route; (c) the retroperitoneal

route, forcefully advocated by Ochsner and Nather.

The abdominal route consists of a high subcostal incision, excluding the uninvolved portion of the peritoneal cavity. The anterior right and posterior right spaces may be so approached.

In the thoracic approach, make an incision with its center in mid-axillary line over the ninth and tenth ribs, resect between 2 and 3 inches of the rib subperiosteally and either pack for forty-eight hours to cause adhesions between the layers of the pleura or suture them together ring fashion, leaving a space for an incision to reach the diaphragm. Incise the diaphragm and insert drains. Serous fluid above the diaphragm is a good indicator of the proximity of the abscess, and is found in from 25 to 30 per cent of the cases. This fluid is not infected unless the abscess has perforated into the pleural cavity.

In the retroperitoneal approach of Ochsner and Nather for which they claim many advantages, especially avoidance of pleural contamination, the twelfth rib is resected, leaving a soft wall on both sides, allowing greater possibility of cavity obliteration. The drainage is from the dependent position; also exploration gives access to the retrocecal, retroperitoneal and perinephritic spaces. In this approach, the pleura which comes down to the twelfth rib must be guarded against, as well as the posterior peritoneum which is continuous with the renal fascia.

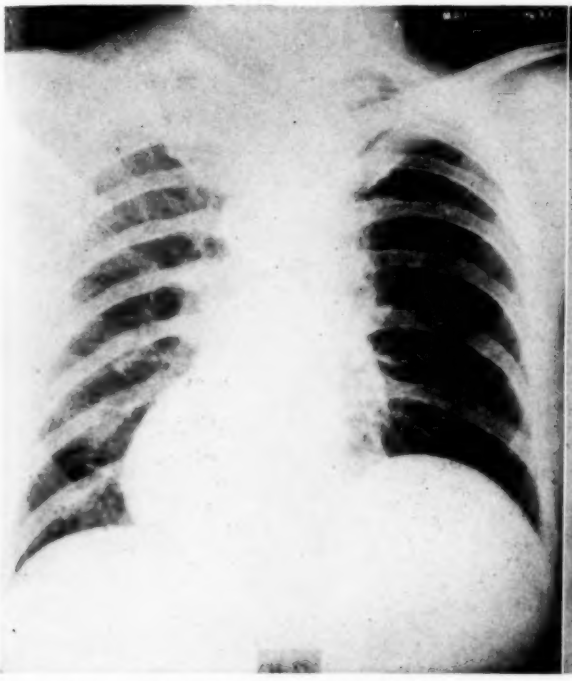

Fig. 7. Case v. Note high right arched dome of diaphragm. Compare with Figure 8 taken three and one-half months later, following successful drainage of a subphrenic abscess.

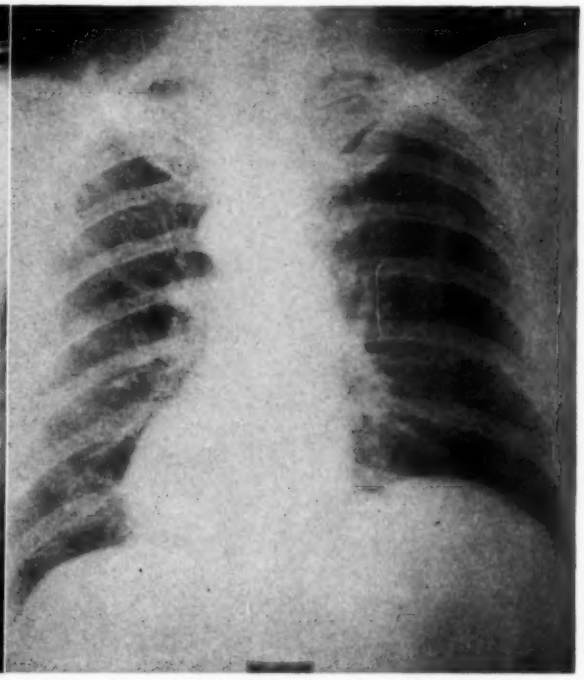

Fig. 8. Case v. Taken three and one-half months after Figure 7. Normal appearing right dome of diaphragm to be compared with Figure 7.

Case 1. D. F., Hurley Hospital, referred by Dr. D. C. Smith. This boy, nine years of age, was admitted to the hospital March 19, 1921. About three weeks previous the patient was taken violently ill with pain in the upper abdomen. This followed an acute sore throat. He coughed moderately, ran a temperature between 101–104°F., pulse 110–128, respiration 36–40, and vomited. Physical examination: He was a very ill appearing boy, the throat was negative, the right side of the chest lagging, and an area of dullness extended to the nipple line and posterior angle of the scapula. Liver dullness slightly below the costal margin was noted. The abdomen was moderately distended and moderately spastic with some flatness in the right hypochondrium and pelvis. There

was no pain in the appendiceal region; it was thought that a mass could be detected in the cecal region. W.B.C. 27,000 polymorphonuclears

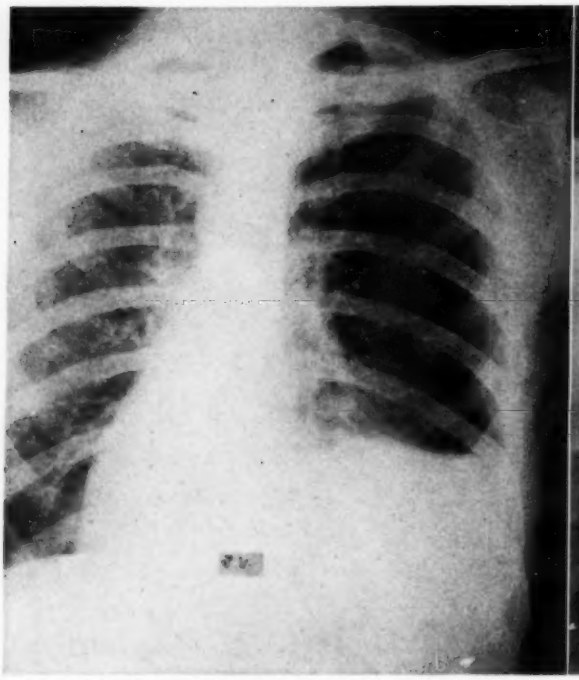

Fig. 9. Case VI. Taken August 24, 1932. High right diaphragm, obliteration of costophrenic angle; note almost right angle of shadow, no doubt due to a pleuritis. Compare with Fig. 10.

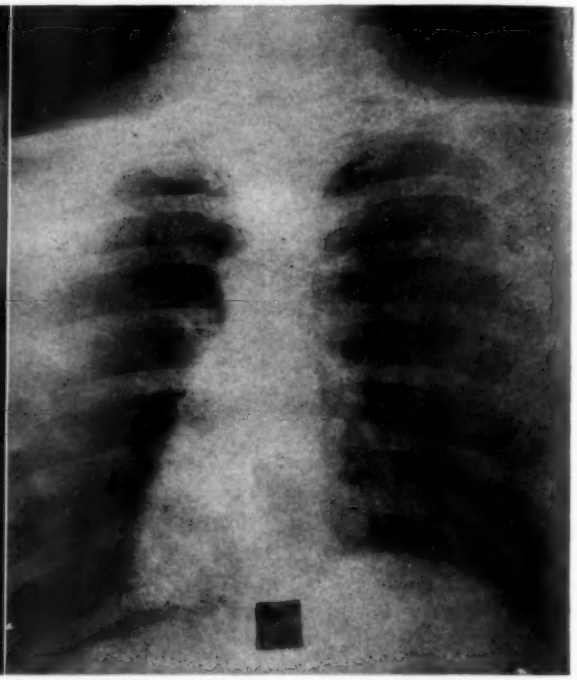

Fig. 10. Case VI. Taken May 18, 1933. Normal height and arch of right diaphragm; note absence of right angle as seen in Figure 9.

88 per cent. Bowel movements occurred only following enemata. A probable diagnosis of ruptured appendix with localized peritonitis was made.

A right rectus incision was made extending upwards. A great deal of pus in the right gutter, with a ruptured retrocecal appendix was found. A mass could be felt in the gall-bladder region. On separating the adhesions between the colon and abdominal wall, a gush of pus under pressure was released with the abscess cavity posteriorly to the liver. The liver was bound down by adhesions and not displaced. One drain through Morison's space to the abscess cavity and drains to the appendiceal region and through a stab wound in the right flank were inserted. He improved somewhat but continued to run a temperature between 100–102°F. Drainage was satisfactory. Three weeks following the primary operation his chest findings were essentially the same as already given, W.B.C. 21,000, polymorphonuclears 90 per cent. *X*-ray studies were made and Dr. Chapel, roentgenologist, reported a diffuse massive effusion in the right chest. The eighth and ninth ribs were resected subperiosteally, the reflected pleura was greatly thickened, a trochar was inserted and pus came out under pressure; the opening was enlarged and a ragged thickened perforation was found in the diaphragm which was enlarged and a tube inserted posterior to the liver and one into the pleural cavity. Dakin solution irrigations were given every three hours. There was profuse drainage for about three and one-half weeks; the tubes were removed; the patient was discharged the eighth week following admittance, with a small sinus in the right chest. The sinus closed a short time afterwards. The patient has been well since.

This case illustrates the possibility of a subphrenic abscess developing following a ruptured appendix prior to operative interference.

Case II. W. J., Hurley Hospital, referred by Dr. J. L. Leach.

A man, thirty-seven years of age, was admitted to the hospital December 26, 1929. For the past year the patient had severe attacks of abdominal pain, right side, otherwise well. About a week prior to admittance, he developed an acute respiratory infection, coughed a great deal and expectorated bloody sputum, complained of a great deal of pain in the mid-

epigastrium, radiating to the right. The pain was relieved by flexing the knees on the abdomen; he vomited often. On admittance the patient had a temperature of 103°F., pulse 130, respiration 32. Physical examination: lungs negative except for a few rales in right chest, heart negative, abdomen rigid with tenderness of right upper abdomen, right thigh held flexed. Extremities were negative. White blood count 25,400; polymorphonuclears 92 per cent urine negative.

The patient was operated on with a preoperative diagnosis of a ruptured appendix. The findings were free fluid in the upper right quadrant with fluid coming from the lesser abdominal cavity. The pylorus was bound down with adhesions, plastic exudate present, the stomach extremely small. The appendix was removed, a drain was put in the lesser cavity and the abdomen closed. A great deal of pus drained and he improved rapidly. He was discharged with the wound still draining moderately, which closed in two weeks. The patient returned to work three months following discharge. Examined in the later part of 1932, the wound was well healed, the patient had gained weight and was feeling well and had had no recurrence of abdominal symptoms.

This case offers an interesting conjecture of whether it was a so-called idiopathic, secondary to a pin point gastric perforation, or a lymphatic infection. If lymphatic, from what region? The pathologist's report of the sectioned appendix was chronic appendicitis and except for a plastic exudate in the region of the pylorus no etiological factors were found in that region for the development of a subphrenic collection of pus in the lesser cavity.

Case III. W. B., Hurley Hospital, referred by Dr. S. Flynn.

A man, forty-one years of age, office worker, was admitted to the hospital October 7, 1930, 3:10 P.M., with a diagnosis of ruptured gastric ulcer of about twelve hours' duration. There was a previous history of medical treatment for gastric ulcer and a history of hematuria of several years' duration. The patient was in moderate shock, temperature 96.8°F., pulse 80, in severe pain. White blood count 11,000 with 74 per cent polymorphonuclears. Urine: albumin, 4 plus, pus cells and numerous R.B.C. No extended examination was possible; the heart and lungs appeared normal. The abdomen was rigid and board-like, the skin cold and clammy. Morphine and normal salt injection were ordered preparatory to operation. He was operated on at 5:40 P.M., closed

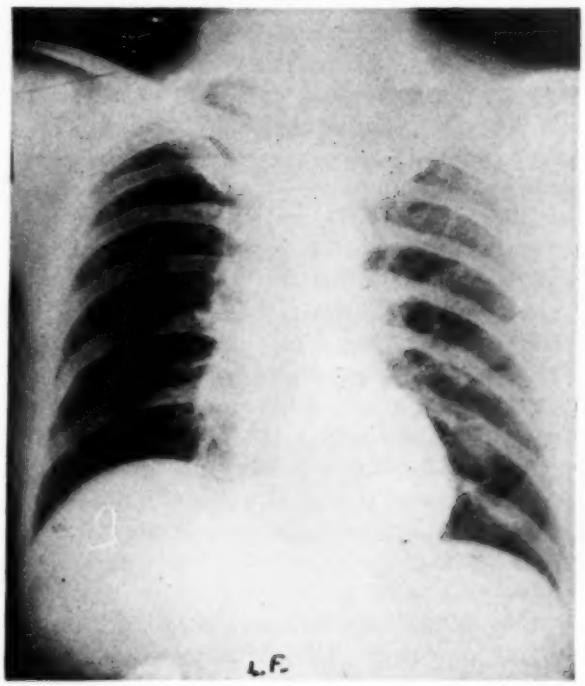


Fig. 11. Case VIII. Taken May 22, 1933, about two months following drainage of tuboovarian abscess. Note high right diaphragm acutely arched. Patient recovered following drainage through posterior route (Nather and Ochsner technique).

at 6:05 P.M.

Findings: There was a great deal of fluid in the right upper quadrant and right abdominal gutter and pelvis, the lesser abdominal cavity containing fluid, a perforated ulcer on the anterior wall of the proximal portion of duodenum. Peritonitis was present; the fluid was removed by suction. The ulcer area was closed and covered with omentum, drainage and closure. The patient's condition was fair. Instructions were given that he receive fluids subcutaneously and per rectum, narcotics as indicated, Fowler's position.

The patient did fairly well; however the temperature went up to 102°F. the fourth postoperative day, but fell to normal on the seventh postoperative day and stayed normal until the tenth postoperative day when it went up again to 102°F. at which time he complained of pain in the upper abdomen and right costal region; hiccough was present. He coughed moderately and expectorated considerably. On examination the wound drained moderately,

sutures appeared tense. A few moist rales were noted in the right posterior chest. Two of the upper stay sutures were released and the patient experienced some relief. The bowels moved with enemata, no vomiting. He appeared quite ill. On the thirteenth postoperative day the patient appeared somewhat dyspneic. Dr. Macduff, roentgenologist, reported "possible bulging of the lower right ribs, heart shadows prominent to the left, left dome of diaphragm smooth and regular. The right dome is not seen, due to a homogeneous dense shadow, obliterating the rib shadow in this region. The right lung above the level of the hilus appears hazy and fussy, suggesting an extensive bronchopneumonia. The right diaphragm is not distinguishable, no information regarding a subphrenic abscess is discernable, although the findings are not incompatible with such abscess by the appearance of the film." Dr. Marshall, in consultation on the same date, found bronchopneumonia, lower right, most likely secondary to an inflammatory condition under the right dome of the diaphragm, advised stimulation, with view of exploration at a later date. At this time the patient's respiration went up to 40, pulse 146, temperature 103°F., dyspnea present. He also developed a dry ringing cough, unproductive, the condition was very poor and exploratory procedure was deferred. The usual supportive measures were administered. On the fifteenth postoperative day, the patient suddenly coughed up an enormous amount of ill-smelling pus and was somewhat relieved; postural drainage was resorted to, but his condition became suddenly worse and the patient expired on the morning following the rupture of the abscess through a bronchus.

Postmortem Findings: There was a small amount of free fluid in the right side of the thoracic cavity, the arch of the right diaphragm is much higher than usual, extending to the third rib. The left diaphragm is normal, no fluid was found in the left thoracic cavity. Both lungs were bound down by numerous fibrous adhesions, which were densest towards the diaphragm posteriorly. On removing the right lung a large quantity of pus exudes from the branch of the main bronchus. The right lung, for the most part, is reddish brown in color and non-crepitant posteriorly. The under surface of the right lower lobe shows two large surfaces of definite necrosis, large areas of lung tissue were destroyed and the cavities filled with necrotic material. Cut surface exudes a frothy purulent material. Left lung: general appearance same as the right except no areas of necrosis present. Marked congestion was present and purulent material exuded on pressure.

On opening the abdominal cavity there was a large hole through the diaphragm continuous with the opening of the right lower lobe and pus exuded from the abdominal cavity into the thoracic communication. This perforation of the diaphragm connects with an abscess cavity between the right dome of the liver and right arch of the diaphragm. On the anterior proximal portion of the duodenum, there was a repaired perforation, covered with gastrohepatic omentum. The lesser cavity was filled with pus and also contained a necrotic serous membrane. The kidneys showed fetal lobulation and appeared pale. The urinary bladder wall is definitely thickened and a definite area of ulceration was present around the internal orifice of the prostatic urethra.

Pathological diagnosis: empyema from perforation of subdiaphragmatic abscess; contiguous lung abscess; terminal bronchopneumonia.

The dramatic sequelae of an early abscess formation with resulting bronchial perforation are well illustrated. The condition was seriously enough considered early in the developmental stage, but at no time following the recognition of the situation was the patient's condition such that exploration could be carried out. Perhaps trochar drainage could have been resorted to, yet this procedure was debatable.

CASE IV. Mrs. M. G., Hurley Hospital, referred by Dr. E. Guile.

The patient was admitted November 25, 1930, with pain in right lower quadrant, of one week duration. W.B.C. 26,400, Polymorphonuclears 94 per cent; Albumin 4 plus. She was operated on November 25, 1930, when a gangrenous appendix was removed, no free pus being found. The appendix was pelvic in location. The first few days the patient ran a very moderate temperature which subsided by the seventh day. The bowels moved with enemas; there was no distention. On the tenth postoperative day the patient complained of pain in the lower right costal region, coughed and vomited. W.B.C. 34,800, polymorphonuclears 92 per cent. There was some tenderness in the lower abdomen, there were a few moist

rales on the right posterior chest, breathing lagged on the right side. She was treated expectantly till the fifteenth postoperative day, when on vaginal examination a bulging was detected in the posterior cul-de-sac, which was drained on that day and a great deal of foul pus evacuated. She continued to drain a great deal, but her temperature ranged between 99° and 101°F. On the twenty-eighth postoperative day she complained of a great deal of pain in the right costal region and soreness in the upper abdomen. She hiccoughed and vomited. Breathing was notably retarded on the right side. There was flatness two finger breadths above the normal liver dullness, latero-posteriorly. The upper abdomen was tender and the right costal arch bulged. X-ray studies, as reported by Dr. Macduff, showed a high right dome of the diaphragm. Heart normal, no lung pathology.

Possible diagnosis: subphrenic abscess. White blood count on that day showed 38,000, polymorphonuclears 92 per cent. The patient was operated on again on the twenty-seventh day following the first operation. A subcostal right rectus incision was made and a large amount of pus was found in the right anterior and posterior intraperitoneal spaces, which were drained through the abdominal wound and through a separate stab incision posteriorly. Drainage was exceedingly good, her temperature subsided and she left the hospital on the fifty-fourth day in good condition.

She was re-rayed June 8, 1933, with right diaphragm in normal position as reported by Dr. William Clift.

Case V. W. McI., Hurley Hospital, referred by Dr. Don Brasie, March 24, 1932.

A man, forty-five years of age, on the day previous developed severe pain in the epigastric region which continued till the next day. He had worked to 5:00 P.M. on the day of admittance when he came home and went to bed. He had never suffered any gastric disturbances, and had always been well except for malaria in 1911, when in the Army.

On the day of admittance, the patient presented the usual picture of an abdominal catastrophe and was operated on at 9:00 P.M. the night of admittance, with a preoperative diagnosis of a ruptured gastric ulcer by another surgeon, who found a small callous ulcer prepyloric. Free fluid was found in the abdomen. The ruptured ulcer was circumscribed with a purse-string suture. One drain led out through the pelvis, and one led out from the foramen of Winslow. The patient's condition was considered poor. He was given the usual postoperative care, hypodermoclysis, etc., and drainage was considerable. He ran a steeple temperature 103–100°F. On the seventh day he began to cough considerably and expectorated a greenis hmucus. He continued to cough a great deal. He was seen by an internist on March 31, 1932, who suggested a diagnosis of postoperative atelectasis or bronchopneumonia.

Retention sutures and drains were removed the thirteenth postoperative day. The temperature came down to between 101–99°F. daily. There was a separation of the wound, omentum visible. The wound was kept strapped and the patient was evidently progressing well. From the seventeenth postoperative day till the thirty-fourth postoperative day, the patient ran an almost normal temperature. He had no complaints, the cough subsided, he ate a light diet, and bowel movements were effective with mineral oil; a complete picture of a patient on the gain. On the thirty-fifth postoperative day the patient complained of pain in the upper abdomen. He did not vomit, there was no distention, the bowels moved with an enema but he felt uncomfortable, ill; the temperature was 100–103°F., there was pain in the right costal region. He was seen by the author in consultation May 6, 1932, on the forty-third postoperative day, with the following record: Very ill-appearing man, gaping wound, right upper abdomen with a small amount of drainage. Stab wound in right inguinal region, not draining, spasticity and mass present in right lower quadrant. Some moist rales and fluid seemed to be present above the diaphragm or liver. W.B.C. 23,000, polymorphonuclears 92 per cent.

Impression: Possible subdiaphragmatic abscess with fistulous tract to lower wound. Advise turpentine stupes and *x*-ray study.

The *x*-ray revealed normal findings, except a somewhat higher than normal right diaphragm, the costophrenic spaces were clear. The roentgenologist felt that the only important finding was the right high diaphragmatic arch and did not think that an absolute diagnosis of subdiaphragmatic abscess was warranted on the *x*-ray findings alone. However, considered with the other findings, an exploratory procedure was deemed advisable with a

probable diagnosis of a subdiaphragmatic abscess.

Operative findings: There was a fistulous tract leading to the right inguinal region towards the pubis. There was an incisional hernia in the right rectus region above the umbilicus. There were many adhesions leading around the right gutter upwards, and when adhesions were broken through posterior to the liver, a gush of fluid came through which was serosanguinous in character. The gall-bladder was greatly distended. There were many adhesions laterally. The left side of the abdomen was comparatively free of adhesions.

The incision was made in the mid-axillary line slightly above the crest of the ileum. The abdomen was entered laterally so that no infection was carried to the unaffected part. The fistulous tract, injected with methylene blue, was found to lead to the right abdominal gutter. A collection of fluid was found under the liver leading from the lesser abdominal cavity. The adhesions were broken through and the abscess cavity drained with a Penrose drain, leading out from a stab wound through Morison's pouch, another drain to the edge of the gastrohepatic ligament and three drains through a suprapubic stab wound. The incision was closed in the usual manner.

The patient's temperature came down abruptly for several days and then climbed somewhat; drainage was good and no anxiety was felt. On May 24, 1932, the fifteenth postoperative day (second operation), a red blood count showed R.B.C., 3,850,000, hemoglobin 75 per cent; the red cells show a slight poikilocytosis and anisocytosis.

He appeared somewhat pasty in color and it was thought that there may be amyloid changes, and with a recent report by B. H. Whitbeck[15] of treatment with liver extract to which was added viosterol gtt. was ordered daily. A red blood count was made on June 3, 1932, the twenty-fourth postoperative day (second operation), with the following report: R.B.C. 4,600,000, hemoglobin 75 per cent, color index 8.

The patient was discharged in the ambulance with the notation: wounds granulating, small amount of drainage, all drains out. He continued to improve, and on August 31, 1932, three and one-half months following his second operation, he was re-rayed.

Dr. Clift, the roentgenologist, reported that the chest was practically normal, the right diaphragm not higher than usual. The patient was fitted with an abdominal support for the ventral hernia and resumed work shortly after. This case illustrates the necessity of correlating all findings for a proper diagnosis.

Case VI. J. V., Hurley Hospital, admitted August 23, 1932, referred by Dr. E. Guile.

This man, aged twenty-eight, with a history of several appendiceal attacks, a week prior to admittance, had an unusually severe attack of abdominal pain and vomiting. He refrained from food, rested and took cathartics. Returned to work on the morning of admittance when he collapsed, was taken home and seen by his physician, Dr. E. Guile, who diagnosed a ruptured appendix and persuaded him to enter the hospital. He presented a picture of a very ill man, and therefore was prepared for operation by the administration of fluids, stimulation and expectant treatment till the next morning. At operation on August 24, 1932, a gangrenous ruptured appendix was removed, as well as a great deal of pus evacuated. There were signs of generalized peritonitis. Drainage was instituted through the incision and a separate suprapubic stab. His postoperative treatment consisted in continuous venoclysis, 4000 c.c. per twenty-four hours for four days, the Fowler position and other supportive measures. His distention subsided, drainage was profuse and he steadily improved, though running a mild temperature. He did not vomit nor hiccough, nor did he have any dyspnea. On the seventeenth postoperative day he suddenly developed a higher temperature and became dyspneic.

Physical examination: The chest showed very limited breathing on the right side, some bulging of the costal arch and flaring as compared to the left side. The abdomen was spastic and tender in the right upper quadrant with some bulging. Drainage was fair. Percussion over the chest showed dullness to the fourth interspace anteriorly, somewhat lower posteriorly. *X*-ray studies, as reported by Dr. Wm. Clift showed a very high right diaphragm running straight across in the upper border, and an obliterated right costophrenic angle. Lung examination was negative. This suggested pathology probably below the diaphragm, believed to be a subphrenic abscess. On September 19, 1932, the twenty-second postoperative day, the original wound was reopened and enlarged upwards and pockets of pus encountered in the anterior

and posterior right intraperitoneal spaces. Drainage was instituted through Morison's space and incision.

The patient improved rapidly and was discharged about five weeks following entrance with some drainage, but greatly improved.

Drainage subsided in the course of several weeks and the patient returned to work at his usual occupation. On May 5, 1933, he was re-rayed with the following report: "At the present time the right diaphragmatic arch has receded and occupies the normal position. The diaphragm shows a normal contour."

Case vii. Mrs. J. H., St. Joseph's Hospital, referred by Dr. J. L. Leach July 5, 1932.

The patient was thirty-two years of age, born in New York State, married ten years, no children. Her father died four years ago of pulmonary Tuberculosis, her mother is living and well; three other children are well. Past history was negative. About two months ago she noticed a painless swelling on the right side of the abdomen which increased a great deal in the last two or three months. With the increase, pain made itself evident with a slight jaundice.

Physical examination: Liver dullness was higher than normal, lungs and heart negative. There was a spherical mass evidently attached to the liver and the right flank felt full, the mass could be moved upward. There was some tenderness in the lower right costal arch and the right muscles were spastic. There were no findings on the left side. Vaginal and rectal examinations were negative. Temperature 99°F., pulse 92, respiration 22, white blood count 10,900, polymorphonuclears 70 per cent, lymphocytes 30 per cent, no eosinophils, color index 8.

A probable diagnosis of an echinococcus cyst of the liver or distended gall bladder was made and an exploratory operation was performed, at which time two large echinococcus cysts of the liver were shelled out from the right lobe, which was thinned out to a shell. The outside capsules were left in situ and hundreds of daughter cysts were liberated.

The patient's condition following the operation was good. For twelve days her condition steadily improved. On the thirteenth day her temperature varied between 99–100°F., with pulse 82–90. The sutures and drains had been removed and she was on a soft diet, with normal bowel movements. On the fourteenth postoperative day, the temperature rose to 103°F. and by the seventeenth postoperative day it varied from 101–104°F.; breathing was labored and the right chest expanded; W.B.C. 17,000, polymorphonuclears 96 per cent, R.B.C. 3,000,000, hemoglobin 55 per cent. An internist saw her in consultation on July 25, 1932, the eighteenth postoperative day. Findings were as follows: Right lobe of liver probably lower than normal, some spasticity in the upper right abdomen with wound draining well. The right lower chest appears enlarged with slight expiratory excursion on the right side. Intercostal spasm is present. Tactile fremitus is normal posteriorly, diminished in front. On percussion there was dullness for a hand's breadth at the base, impaired resonance above this for a hand's breadth, no rales. The whispered voice sounds diminished in front and laterally, but almost normal posteriorly; otherwise, normal findings. From these findings a diagnosis of subphrenic or intrahepatic abscess was deemed probable. No *x*-ray examination was available at the time and an exploratory puncture with operative measures, if needed, was proposed.

On July 29, the twenty-second postoperative day, 2 inches of the eighth and ninth ribs were resected under local anesthesia, the pleura was dissected up and following the introduction of a trochar, through which serous pus was obtained, a large subphrenic abscess was drained.

On culture pure streptococcus was found. Following the drainage there was a sudden drop in temperature and the patient seemed relieved, but on the second day the temperature rose to 105°F., breathing became difficult and she grew steadily worse, though good drainage was present. The patient died on August 5, 1932.

The pathologist reported that there was an old inflammatory process in one of the large cysts.

Whether this case presented an intrahepatic abscess that perforated into the subphrenic space, or whether it was a subphrenic abscess to start with, was not possible to determine.

There was no post mortem. At no time was there any odor from the discharge.

Case viii. Mrs. L. F., first admitted March 4, 1933, referred by Dr. N. A. Andrews.

The patient, aged twenty-six, married, was operated on March 15, 1933, by Dr. W., at

which time a tubo-ovarian abscess was drained abdominally and a diagnostic curettage was done. She progressed moderately well, ran a fever for three weeks with a rather fast pulse. Six days postoperatively the patient complained of pain in the right upper quadrant and along the right costal margin; there was no shifting of the liver dullness. She was discharged on April 11, 1933, with drainage slightly above normal, generally improved. She was readmitted May 22, 1933 with a temperature 103°F., pulse 160, W.B.C. 21,000 polymorphonuclears 89 per cent, R.B.C. 3,100,000, hemoglobin 45 per cent, urinalysis negative. There was a palpable movable mass in the right epigastric region. The right lower chest appeared full, there was a suggestion of an increased costal flare on the right side. Respiratory movements were not painful, though somewhat retarded on the right side. She did not cough, but experienced periods of hiccoughing. There were no distinct lung findings. She appeared extremely ill and showed the effects of prolonged suppuration. The original operative wound was well healed. X-ray studies as reported by Dr. Wm. Clift were as follows: A stereogram of the chest shows some elevation of the right diaphragm and obliteration of the costophrenic space on that side. Examination of the kidney region was negative.

The findings were not wholly typical but we suspected the presence of a subdiaphragmatic abscess with some pleural involvement. The patient was operated on under nitrous oxide and local infiltration anesthesia. The twelfth rib was resected, the wound was deepened to the renal fascia, which was pushed upward, the pleura was dissected upward and medially. The peritoneum was separated from the diaphragm and the peritoneal cavity was entered posteriorly. There were adhesions between the liver anterior and posteriorly. Serosanguinous serum was encountered in the right posterior intraperitoneal space, and a great deal of pus in the right anterior intraperitoneal space. Ample drainage was introduced and the patient put on supportive postoperative treatment. At present, four weeks following the procedure outlined, the patient has left the hospital. Temperature has been normal three weeks; W.B.C. 9,000, polymorphonuclears 76 per cent; R.B.C. 700,000, hemoglobin 75 per cent, wound healed well.

## SUMMARY

1. Eight cases of subphrenic abscess are presented, and pertinent literature reviewed.

2. The condition, though uncommon, still must be considered following intra-abdominal infections and intra-abdominal surgical interference.

3. The mortality has been greatly decreased of late years, due to earlier diagnosis and improved technique.

4. In the author's series of 8 cases there were 2 deaths, or a mortality rate of 25 per cent.

I wish to acknowledge my sincere thanks to Drs. Wm. Clift and Bruce Macduff, roentgenolists, for valuable guidance and cooperation, and Mr. Homer M. Shively for the painstaking photography of the presented plates.

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# INFUSION REACTIONS

## WITH SPECIAL REFERENCE TO "SPEED SHOCK"*

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THE infusion or venoclysis has become today an integral part of preoperative and postoperative care of surgical patients. To Pepys, writing in his famous diary over 260 years ago, intravenous therapy was regarded as an experimental curiosity. Keith,[1] in reviewing the history of intravenous medication, traces its origin to the injection of drugs by Boyle and Wrenn to experimental animals. The first direct transfusion from animal to animal was done by Richard Lower in 1665. When the Asiatic cholera epidemics ravaged Western Europe in 1831–32, Latta, a Leith, Scotland, doctor, gave "saline infusions" to patients in severe collapse, with good results. During the past quarter of a century, the work of Carrel, Crile, Lindeman, Lewisohn and Unger on blood transfusions has perfected the technique of intravenous therapy. Today, it is simple and without undue danger.

With the widespread use of the infusion in the armamentarium of the clinician and surgeon, there has arisen a new interest in solving the etiological factors involved in the untoward reactions that have, in the past, all too frequently attended the administration of fluids by the venous route. Numerous workers have attacked the problem of reactions from a variety of angles. Individual susceptibility, severity of the illness, solutions per se, rubber tubing, glassware, temperature of solution, hydrogen ion concentration, and speed of injection, have all been carefully scrutinized by a host of independent workers.

We will not enter into a detailed discussion of all of the afore-mentioned possibilities. Our purpose here is principally to consider the role played by the speed of injection in producing infusion reactions. Of late there has been much agitation on this subject and in a series of reports Hyman et al.[2] have described the syndrome of "speed shock," resulting from rapid intravenous injections. They are of the belief that a rapid injection of any molecule into the vein may result in widespread systemic disturbances. Using animals (dogs, cats, rabbits, and monkeys), they injected a variety of substances, from hypotonic, isotonic and hypertonic solutions to sugars, colloids, gels, suspensions and drugs. The rate of flow varied from 3 to 10 c.c. per minute, by gravity method.

Irrespective of the nature of the agent, its dose, concentration, or the functional state of the animal, Hyman and his coworkers state they were able to elicit in whole or in part the clinical syndrome to which they refer as "speed shock." The major symptoms of these reactions, occurring forty to sixty seconds after the injection, were a rapid fall in blood pressure, respiratory irregularities, incoagulability of blood, and even death. To them, the reaction was based on a technical error and not a physical, chemical or immunological entity, and therefore the prophylaxis was a slow intravenous drip with a rate of flow of 2 or 3 c.c. per minute. In more recent papers,[3] they cite clinical applications and describe the apparatus used.

It is a not infrequent occurrence, after a post-infusional chill, to hear some member of the staff ask how fast the venoclysis was given, the direct implication being that speed caused the reaction. With this

* From the Surgical Service of the New York Post-Graduate Hospital.

work as a background, and with an open mind, the writer recorded a series of infusions as performed in the routine care of patients on the surgical wards of the New York Post-Graduate Hospital. In the accompanying table an analysis of each case is recorded.

All of the infusions were administered, and the clinical data obtained and recorded, by the writer so that variations in technique can be ruled out. In every case one of the antecubital veins of the arm was used; a 17 gauge 1½ inch needle inserted and the solution allowed to run by gravity from a glass bottle suspended from a 6 foot standard. The solutions used varied both in bulk and in composition.

The severity of disease varied in this series from simple administration of preoperative supportive fluids to postoperative shock, as witnessed in Case I. There appeared to be no relation between the severity of the disease process and the reaction to infusion. In fact, Patient I, perhaps the sickest, with severe postoperative shock, feeble pulse and low blood pressure, showed the greatest clinical improvement from a 10 per cent glucose infusion, at the rate of 94 c.c. per minute.

The indications for the infusions were diverse. The giving of fluids postoperatively formed the chief group. Also included were those for acute shock, for progressive bleeding, preoperative fluids, and therapeutically as in Case II for endarteritis obliterans. The three reactions recorded all occurred in patients whose fluid intake by mouth was insufficient, the venous route being utilized for supplying additional water and nourishment.

The amount of solution administered ranged from one infusion of 300 c.c. to two of 1500 c.c. each. For the most part they bulked from 750 c.c. to 1000 c.c. The solutions included normal, 2 per cent and 5 per cent saline; 3, 5, and 10 per cent glucose. Parenthetically it might be stated that these solutions were made up in the operating room under the direction of a graduate nurse in charge of this particular department. Singly distilled water was used and Dextrose Merck, C.P. anhydrous, used in making up the glucose in saline solutions.

In the process of preparation, the solutions are tested by a special indicator-colorimetric method to insure a proper pH. The prepared flasks containing the desired solutions are stoppered and autoclaved for forty-five minutes under 5 pounds' pressure. Glucose solutions are kept on the shelf up to seven days and if not used by that time, are discarded. Saline solutions are resterilized after seven days and used again. Incidentally, the only real chill that occurred in this series, in Case IV, came after using 2 per cent saline which was freshly made up on short notice.

As a matter of interest, three transfusions are included in the series. All were given by Dr. Unger and the observations recorded by the writer. Dr. Unger, using his own instruments in administering thousands of transfusions, states that speed of injection plays a negligible role in the production of reactions from transfusion, and he has never seen the manifestations of the syndrome of "speed shock" from too rapid injection of blood.* In Case XXIV, two syringes were worked on the Unger machine at the same time, enabling 500 c.c. of blood to be transfused in three minutes, a rate of 166 c.c. per minute. Case XXV was transfused at the rate of 177 c.c. per minute. Neither patient showed any immediate or remote reaction to the transfusion.

The temperature of the infused solutions was not accurately measured but was approximated at 100–105°F. Matas[4] and Horsley[5] are both of the opinion that temperature of solution is insignificant. If the patient has a high temperature, Matas gives the solution at room temperature; if low, the fluid is given at 100–104°F. at the vein. Titus,[6] on the other hand, believes that keeping the temperature at the vein between 100–110°F. is important,

* Personal communication.

and he has devised a special electric heater to keep it at this point.

We now come to the question of speed of administering infusions. It has been widely discussed and apparently the pendulum has swung to the extreme conservative side, with special emphasis upon the drip method of venoclysis. As a result of the cry that rapid infusions are dangerous to the health of the patient, some physicians, fearing the consequences, will only give them via the drip method. Only when the patient is in extremis will a rapid infusion be given by them, and then with alarm at the possible sequelae of the speed of injection.

The work of Hyman has already been referred to. So sure are he and his coworkers of the unfavorable role of velocity, above all other factors, that they conclude that, "irrespective of the temperature of the fluid or the vehicle employed, an intravenous drip whose velocity does not exceed 2–3 c.c. per minute, should be completely devoid of any general reaction." Matas advised an average rate of 40–60 drops per minute, with alterations to 30 drops or less with rising blood pressure, and continuous flow when there is greater need of stimulation. Incidentally, after analyzing all factors concerned, Matas concluded that the reactionary chill and fever "would seem to be a matter of individual susceptibility."

Hendon[7] alludes to chills and sudden elevations of temperature which regularly occur when solutions are suddenly or rapidly introduced directly into the circulation. Titus, in conjunction with Dodds, advises a rate of 3 c.c. per minute for 25 per cent glucose and 7.5 c.c. for 10 per cent glucose. They have devised a special apparatus to regulate the speed of injection and the temperature of the solution. Horsley, while advising a rate of 75 to 200 c.c. per hour by means of continuous intravenous injection, states that as much as 400–500 c.c. can be given in a few minutes in cases of shock or hemorrhage where the blood pressure is below normal. He noted only 3 or 4 reactions in the last two years attributable to intravenous injections, since using purified dextrose.

With these observations and admonitions, the problem of velocity of infusing physiological solutions was undertaken. Pulse, respiration, blood pressure and temperature readings were taken before and after the infusion, together with a record of the time consumed in actually giving the amount of solution ordered. As will be noted from the accompanying chart, the rate of injection varied from 38 c.c. per minute to 150 c.c. per minute. In the case of one of the transfusions, 400 c.c. was injected in 2¼ minutes, making a rate of 177 c.c. per minute. All of the infusions were administered by gravity, whereas the transfusions were given by the injection method of Unger.

No untoward reactions affecting pulse or respiration occurred in the series, the writer standing by from the start to finish of the procedure and seeing the patient at frequent intervals for the next twelve hours. Ten of the cases showed a slight drop in pulse rate, although the volume was perceptibly improved. Eight showed a pulse rate rise, none over 20 beats per minute, and seven showed no change at all. The change in respiratory rate was negligible. The majority, nineteen, showed a rise in systolic blood pressure, the greatest being in Case I, suffering from marked postoperative shock. Three showed a fall in blood pressure and a like number remained stationary. Diastolic readings practically paralleled the systolic variations.

In recording the temperature readings, the natural postoperative temperature rises have to be considered. Thus, in Case XXV, a boy with a streptococcus bacteremia and a previous "spiking" temperature record, had a 3.2° rise after transfusion, but without any chill or subjective discomfort. Patient I, previously referred to, rallied from his shock with a 1.2° rise. Only Patient III had a definite chill which came on forty-five minutes after the completion of the infusion and lasted

AN ANALYSIS OF 25 CONSECUTIVE INTRAVENOUS ADMINISTRATIONS

| | Name-Chart | Diagnosis | Indication for Infusion | Amount & Nature of Solution | Time (Minutes) | Rate C.c./Min. | Sex | Age | Wt.-Lbs. | Temp. | Pulse | Resp. | B.P. | Physical Condition | Reaction |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I | M. M. #88445 | Temporal bone flap for old hematoma | Postoperative shock | 750 c.c. 10% Glucose | 8 | 94 | M | 35 | 145 | *97.8 | 132 | 18 | 90/60 | Poor | |
| | | | | | | | | | | *99.– | 124 | 16 | 140/70 | Better—Full Pulse | |
| II | E. C. #87779 | Endarteritis obliterans | Therapeutic for vasodilatation | 300 c.c. 5% Saline | 2 | 150 | M | 58 | 130 | 99.6 | 92 | 20 | 175/100 | Good | |
| | | | | | | | | | | 99.8 | 92 | 20 | 175/90 | " | |
| III | R. W. R. #90571 | Acute appendicitis; appendectomy | Postoperative fluids (nausea and vomiting) | 1500 c.c. 2% Saline | 20 | 75 | M | 34 | 130 | 100.2 | 90 | 25 | 130/80 | Fair | Mild chill for 10 minutes, 45 minutes after infusion; Temp. 101°F. |
| | | | | | | | | | | 101.2 | 105 | 25 | 110/70 | " | |
| IV | " | " | " | 1500 c.c. N/Saline | 25 | 60 | " | " | " | 101.2 | 100 | 20 | 110/80 | Good | |
| | | | | | | | | | | 101.6 | 100 | 22 | 110/70 | " | |
| V | O. S. #90564 | Metastatic carcinoma; cholecysto-gastrostomy | Postoperative fluids (vomiting) | 1000 c.c. N/Saline | 15 | 66 | M | 55 | 155 | 100.2 | 96 | 28 | 135/85 | Good | |
| | | | | | | | | | | 100.6 | 92 | 30 | 148/95 | " | |
| VI | R. B. #90653 | Acute cholecystitis; cholecystectomy | Postoperative fluids (rapid, irregular pulse) | 800 c.c. N/Saline | 21 | 38 | F | 26 | 145 | 102.– | 140 | 28 | 96/68 | Fair | |
| | | | | | | | | | | 101.8 | 120 | 28 | 110/70 | Improved | |
| VII | P. G. #90519 | Pregnancy; bilateral pyelonephritis; abortion | Postoperative bleeding | 900 c.c. 10% Glucose | 10 | 90 | F | 37 | 150 | 98.8 | 100 | 20 | 132/70 | Fair | |
| | | | | | | | | | | 99.4 | 120 | 20 | 135/75 | Better Pulse | |
| VIII | M. R. #90668 | Chronic cholecystitis; cholecystectomy | Postoperative fluids | 800 c.c. N/Saline | 9 | 89 | F | 35 | 130 | 100.4 | 92 | 28 | 132/85 | Good | Chilliness (no actual chill) for 5 minutes 70 minutes after infusion without temperature rise |
| | | | | | | | | | | 100.8 | 108 | 30 | 134/82 | " | |
| IX | N. C. #90651 | Subacute appendicitis; appendectomy | Postoperative fluids (vomiting) | 800 c.c. 5% Glucose | 9 | 89 | M | 43 | 125 | 100.8 | 112 | 20 | 130/100 | Good | |
| | | | | | | | | | | 99.– | 112 | 20 | 135/90 | " | |
| X | A. M. #90565 | Duodenal ulcer | Preoperative fluids | 750 c.c. 5% Glucose | 8 | 94 | M | 42 | 122 | 98.4 | 72 | 20 | 100/70 | Good | |
| | | | | | | | | | | 98.– | 66 | 20 | 100/65 | " | |
| XI | " | " | " | " | 8 | 94 | " | " | " | 98.4 | 72 | 19 | 114/74 | Good | |
| | | | | | | | | | | 98.8 | 72 | 19 | 122/72 | " | |
| XII | " | " | " | " | 8 | 94 | " | " | " | 97.6 | 84 | 20 | 112/70 | Good | |
| | | | | | | | | | | 98.4 | 72 | 20 | 108/66 | " | |
| XIII | H. M. #90960 | Hyperthyroidism; thyroidectomy | Postoperative fluids | 800 c.c. 5% Glucose | 13 | 61 | F | 41 | 124 | 99.– | 102 | 22 | 110/50 | Good | |
| | | | | | | | | | | 99.2 | 92 | 22 | 150/45 | " | |
| XIV | M. S. #90889 | Carcinoma of colon; resection | Postoperative fluids | 800 c.c. N/Saline | 7½ | 106 | F | 28 | 99 | 101.– | 104 | 23 | 110/60 | Good | Slight chilliness (no actual chill) for 5 minutes 90 minutes after infusion, temp. 103°F. |
| | | | | | | | | | | 103.– | 88 | 24 | 136/76 | " | |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| XV | J. V. #91205 | Gastric ulcer; duodenal ulcer; gastric resection | Postoperative fluids | 1000 c.c. N/Saline | 13 | 76 | M | 37 | 175 | 99.4 | 88 | 20 | 146/88 | Good | |
| | | | | | | | | | | 101.4 | 88 | 20 | 155/90 | " | |
| XVI | " | " | " | " | 12 | 83 | " | " | " | 101.4 | 120 | 24 | 170/90 | Good | |
| | | | | | | | | | | 102.2 | 120 | 24 | 174/86 | " | |
| XVII | " | " | " | " | 13 | 76 | " | " | " | 104.6 | 120 | 25 | 145/85 | Fair | |
| | | | | | | | | | | 102.8 | 124 | 25 | 156/84 | Good | |
| XVIII | " | " | " | " | 14 | 71 | | " | " | 102.8 | 100 | 24 | 144/84 | Good | |
| | | | | | | | | | | 103.— | 104 | 25 | 152/80 | " | |
| XIX | G. S. #91260 | Cholecystitis and lithiasis; cholecystectomy | Preoperative fluids | 750 c.c. 10% Glucose | 13 | 57 | F | 46 | 150 | 98.4 | 80 | 19 | 110/70 | Good | |
| | | | | | | | | | | 98.8 | 92 | 20 | 122/70 | " | |
| XX | E. H. #91337 | Acute cholecystitis; cholecystectomy | Postoperative fluids | 800 c.c. 5% Glucose | 9 | 89 | M | 38 | 149 | 99.6 | 72 | 22 | 130/90 | Fair | |
| | | | | | | | | | | 99.8 | 84 | 22 | 140/80 | Good | |
| XXI | " | " | " | " | 8½ | 94 | " | " | " | 99.8 | 92 | 21 | 130/85 | Fair | |
| | | | | | | | | | | 100.— | 88 | 22 | 142/75 | " | |
| XXII | V. T. #91419 | Chronic cholecystitis; cholecystectomy | Postoperative fluids | 1000 c.c. 3% Glucose | 10 | 100 | M | 64 | 130 | 99.6 | 72 | 18 | 124/66 | Good | |
| | | | | | | | | | | 99.4 | 72 | 19 | 134/72 | " | |
| XXIII | M. O. #90776 | Cardiorenal disease; secondary anemia | Anemia | 500 c.c. Whole blood | 5½ | 90 | F | 34 | 130 | 99.— | 104 | 24 | 220/110 | Good | Transfusions by Doctor Unger |
| | | | | | | | | | | 100.2 | 120 | 26 | 240/115 | " | |
| XXIV | M. G. #90769 | Fibroid uterus; menorrhagia | Anemia | 500 c.c. Whole blood | 3 | 166 | F | 51 | 150 | 99.6 | 100 | 20 | 135/65 | Good | |
| | | | | | | | | | | 100.— | 84 | 20 | 130/75 | " | |
| XXV | A. F. #90429 | Streptococcus infection; leg | Anemia | 400 c.c. Whole blood | 2¼ | 177 | M | 10 | 69 | 100.4 | 120 | 20 | 92/64 | Good | |
| | | | | | | | | | | 103.6 | 108 | 22 | 105/66 | " | |

* Readings before and after infusion.

for ten minutes. The temperature, when taken one-half hour after the chill, showed a rise of 1°. In Cases VIII and XIV, where chilliness rather than actual chill appeared, the intervals between infusion and subjective discomfort were seventy and ninety minutes, respectively. Each episode lasted for five minutes, with temperature rises of 0.4° in one and 2° in the other, remembering, however, that she had had a resection of the colon just a few days before. In all of the cases the general condition of the patient was no worse while in most a decided improvement was apparent.

Woodyatt, Sansum and Wilder,[8] and later Wilder and Sansum,[9] studying sugar tolerance and utilization and the rate of infusion, concluded that roughly 0.8 gm. of glucose per hour per kilo body weight could be given without glycosuria. A man weighing 70 kilos would, therefore, require 63 gm. of glucose per hour before showing a glycosuria. This work would favor the slow infusion of glucose solution when intended solely for nourishment. However, where the dual effect of quickly making up circulating blood volume plus nutrition is desired, it would be more logical to hasten the infusion. The physiological glycosuria and the transient glycemia has not been shown to be detrimental to the body and, furthermore, one can be assured that all the glucose the body tissues can utilize has been supplied. Also, when glucose is used as a hypertonic solution to reduce intracranial pressure or to combat anuria, it would seem that the concentrated effect would be nullified by a slow infusion.

Concerning the cause for the majority of post-infusional reactions, we are inclined to look upon something in the solution as the trouble-maker. Ten years ago, Dr. Florence Seibert[10] revealed that toxic products of contaminating bacteria ("pyrogenic" or reaction-giving substances) constantly gave systemic symptoms in a series of experimental animals and in humans. She showed that the offending agent could be present even though the bacteria were destroyed by sterilization of the solution. Her work has more recently been confirmed by Rademaker,[11] who has re-evaluated the various causes commonly given as reaction-producers.

Using a portable quinhydrone pH determining unit, Rademaker recorded pH readings on 55 infusions, concluding that salines of alkaline pH were more prone to give reactions. The line of division was a pH of 7.05. Accordingly, solutions were classified as pyrogenic or non-pyrogenic. To him, the causal factor appeared to be an alkaline, non-volatile substance, the elimination of which was effected by a single distillation in a specially devised apparatus, immediate sterilization and absolute sealing. A water trap in the distilling process prevented the mechanical carrying over of the toxins, while the immediate sterilization and sealing prevented bacterial growth. Triple distillations were found to be unnecessary if the foregoing routine was carried out.

Rademaker has shown that, irrespective of rubber tubing, glassware, glucose or saline per se, temperature, or speed of injection, he could produce reactions with pyrogenic solutions and avoid them by using non-pyrogenic fluids. Thus, 1000 c.c. of non-pyrogenic solution was given in ten minutes without reaction, while a similar amount of pyrogenic solution given in an hour, produced a reaction. Similarly, non-pyrogenic solutions were given at 20°C. and at 110°F. without reaction and even after rubber stoppers were boiled in this solution until it smelled strongly of rubber, it was administered without any ill-effects.

Perkins[12] has surveyed the situation from the standpoint of the hospital administrator. Concerning the question of velocity, bulk and temperature as causes of reactions, factors governed by the clinician, he states that "experience does seem to show that it is the pyrogenic factor rather than velocity that causes reactions." By stringent attention and care in the distillation of the water, the use of pure dextrose, the careful washing and cleansing of glassware and rubber tubing, and the steriliza-

tion and sealing of the solutions, Perkins has reported the preparation and administration of 196,828 c.c. of fluids intravenously, within a month, without a reaction of any kind, adding that the day before the new still had been installed three severe reactions had occurred.

From data gathered at the Hospital of the University of Pennsylvania, Rademaker[13] has more recently recorded observations made since the installation of new apparatus and centralization of the work of preparing the intravenous solutions. He reported an incidence of reaction of 0 to 4 per cent with an average monthly consumption of 600 liters of solution, this in contrast to a 30 per cent reaction incidence with an average monthly consumption of only 40 liters per month, prior to the reorganization of the department.

## CONCLUSION

This is not a brief for the rapid infusion of any solution into the body. Rather, it is an attempt to show that the role of velocity does not play a clinically perceptible part in administering fluids intravenously. We have not seen the syndrome described by others as "speed shock," despite what to some might seem like phenomenal rates of injection. True, our series is limited to 25 consecutive intravenous administrations, but because of the consistent absence of any signs of reaction from velocity per se, additional cases were considered superfluous.

A brief consideration of the role of other reaction-giving factors has been presented with the implied conclusion that the chief source of trouble lies in the preparation of the solution and the articles used in its administration. We feel that fluids intravenously should be pushed as indicated: very rapidly for replenishing sudden loss of blood volume as in hemorrhage and shock, and slower, as by drip, when supplying nutrient materials to the body tissue over long periods of time. Finally, it must be clear that infusion reactions can be, and are, reduced to a minimum by adequate facilities and careful supervision in a capably staffed central supply room, before the infusion set reaches the patient's bedside.

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# BACTERIAL INVASION OF THE BLOOD STREAM*

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TWENTY-FIVE years ago I had my interneship. We used to see many cases of protracted and severe fever, or of obvious "sepsis." Some of them we recognized easily by clinical observation, cases of typhoid fever, malaria, postpartum or wound infection. Others remained a mystery to us until the autopsy, and sometimes even then. We would watch the continued fever or the chills, the peculiar skin eruptions, the jaundice, the swollen joints, cardiac murmurs, progressive anemia, enlarged spleen or other manifestations. We were seldom able to make an exact diagnosis as to the infecting agent and the mechanism of its entry, and therefore seldom able to apply suitable treatment. Today this situation is greatly changed.

After I had finished my interneship I had the good fortune to spend an additional year working in a laboratory where Dr. Libman was at the time actively developing the use of blood cultures in diagnosis. There was unfolded to me the variegated clinical picture of the general infections, and the extraordinary amount of valuable information that can be derived from blood cultures. I have never ceased to be interested in this field. I propose to give a brief discussion of some aspects of those diseases in which bacterial invasion of the blood plays an important role.

## I. HOW DO BACTERIA ENTER THE BLOOD?

What is the meaning of the finding of bacteria in the blood? Do they actively multiply there as they do in other tissues?

There are two general methods by which bacteria penetrate the blood: (1) lymphatic drainage from local lesions; and (2) direct invasion of blood-vessel walls, usually with production of lesions of the vascular endothelium.

Each method is characteristic of certain bacteria. There are some organisms which according to circumstances may invade the blood stream by either method. In many instances the exact mechanism of the original blood invasion can no longer be determined but the bacteremia is kept up by a secondary focus within the vascular stream such as an endocarditis or thrombophlebitis.

Thus the hemolytic streptococcus when found in the blood is usually being fed into it either from a thrombus or other endovascular lesion. But in some conditions, as for example erysipelas, it may enter the blood stream by the lymphatics.

The original mode of entry of the nonhemolytic streptococcus is not clear. It is believed to reach the blood stream from some indolent chronic focus of infection such as paranasal sinuses, tonsils, peridental tissues. But when found in the blood in sufficient numbers to be cultured it almost invariably is being supplied to the blood stream by infected heart valves.

The Staphylococcus aureus usually invades the vessel walls directly. The bone marrow on account of its enormous vascularity is reckoned as part of the vascular system.

The pneumococcus, the occurrence of which in the blood in pneumonia is of such great prognostic and therapeutic importance, enters the blood stream most commonly without producing lesions of the larger vessels. It seems to have relatively

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little power of penetrating the walls of larger blood vessels, as illustrated by the fact that in mastoiditis it does not produce a sinus thrombosis. This, however, does not apply to the pneumococcus type III (formerly known as the Streptococcus mucosus) which has great invasiveness for the vessels and behaves in this regard exactly like the hemolytic streptococcus.

The behavior of the meningococcus is very interesting. The work of Herrick and others indicates that most cases of meningitis are initiated by a transient meningococcus bacteremia. If blood cultures are made early enough the organisms can be found in the blood stream in the great majority of cases. After this initial invasion the bacteria settle down in their place of predilection, the meninges, and the blood becomes free of them. But in many, and particularly the more severe cases, a secondary feeding into the blood stream by the meninges, probably from the lymphatic channels, occurs. The meningococcus is believed to enter the blood stream in the first place from the nasopharynx but the exact mechanism of this invasion is not known.

Beside the ordinary type of meningitis there are two extremely interesting and clinically characteristic types of meningococcus blood-stream invasions. The one is subacute meningococcemia which bears a close clinical resemblance to subacute bacterial endocarditis and which is generally regarded as due to an infection of the heart valves. In spite of the fact that in this disease meningococci can be demonstrated to circulate in the blood for weeks and often for months, meningitis only occasionally occurs as a complication. The other form of meningococcus blood invasion is acute fulminant purpuric maningococcemia. In this disease, almost always fatal within three days, the blood stream is suddenly invaded (by a mechanism which has not yet been discovered), with such enormous numbers of meningococci that they usually can be easily seen in the leucocytes on direct smears of the blood from the finger tip. They are easily demonstrable in smears from the skin hemorrhages. It is interesting that in the more fulminant of these cases there is no meningitis. In the cases in which the patients live three or more days, and in the rare cases of recovery, a meningitis often develops.

The exact mechanism of the invasion by the gonococcus is also not entirely clear. In the male, blood-stream invasion seldom occurs unless there are complications in the more vascular organs such as the epididymis or the prostate gland. In the female, blood-stream invasion not infrequently occurs in spite of the fact that the local lesions are so trivial that they are hard to find. Except when the gonococci happen to light on the heart valves their invasion of the blood stream is usually transient, and it is only in the early stages of "gonorrheal rheumatism" as a rule that one obtains a positive blood culture. The organisms hardly ever invade the blood stream from the gonorrheal joints themselves. On the other hand gonorrheal endocarditis produces a prolonged and characteristic type of fever with chills. It has a very high mortality.

There is a group of organisms including typhoid and paratyphoid bacilli, and the Brucella group which characteristically invade the blood stream from the gastrointestinal tract. The exact mechanism of invasion is not completely understood but it is most likely, at least in the case of typhoid, by way of the Peyer's patches and the solitary lymphoid follicles of the intestinal wall. In the case of typhoid fever the bacteria are usually only found in the blood during the first few weeks of the disease. After this, although the lymphatic lesions are no less in evidence, the defensive power of the blood is either so great that the bacteria fail to enter, or they are killed off as fast as they do enter the blood. On the other hand relapses are usually ushered in by a fresh invasion of the blood stream.

The colon bacillus and to a certain extent the Bacillus pyocyaneus, although their natural habitat is not the urinary tract, usually reach the blood stream by way of the bladder, urethra or kidneys. In recent years it has been shown that communication between the renal tubules and the blood stream can very easily be established by slight back pressure.[1] The severe chill and transient bacteremia with the colon bacillus or hemolytic streptococcus which so often follows genitourinary manipulations is in all likelihood due to this mechanism.

There is a group of somewhat rarer infections, such as those due to Bacillus tularensis, Bacillus mallei and Bacillus anthracis, in which blood-stream invasion usually occurs from some small local (often traumatic) lesion. As a rule anaerobic general infection from wounds occurs in badly lacerated or contused injuries.

With regard to the bacillus of tuberculosis, anatomical studies have shown that when it enters the blood stream it almost always does so by the direct rupture of a tuberculous lesion through the endothelium of a blood vessel. Recently introduced methods make it possible to grow the tubercle bacillus from the blood stream more frequently than formerly.[2]

## II. DO BACTERIA MULTIPLY IN THE BLOOD?

Until recently it was assumed by most writers that bacteremia means an infection of the blood stream in the same sense as cellulitis means an infection of the tissues. As the result, especially of the work of Schottmüller and of Libman, as well as of numerous experimenters, we now know that this is not the case. In a general way and with a few rare but important exceptions it may be said that bacteria found in the blood do not multiply there but are in transit after having entered the blood stream at some point in the vascular system. They circulate in the blood for a variable and probably not very long time and are then killed and removed from the blood.

On what evidence is this conception founded?

First, the number of organisms found in the blood stream in practically all human diseases is relatively small as compared with the countless millions which are produced by bacteria within a few hours in any suitable culture medium. It is only in postmortem blood (that is, when the defenses of the body have ceased to function), that such myriads of bacteria are found. In this regard most human disease is quite different from certain experimental animal blood infections in which it is possible that there may be active growth of organisms in the animals blood stream. The only human disease that I know of in which conditions are found approaching those found in experimental animals is the acute fulminant purpuric meningococcemia to which I have already referred. In this disease uncountable numbers of organisms are found in every blood smear.

Second there is evidence, experimental and clinical, that bacteria which obtain entrance to the blood stream are rapidly removed. Experimentally this has been shown again and again by a number of workers since Wysokowitch's early demonstration in 1882. Libman and Celler,[3] in 1909 showed that in sinus thrombosis the circulating bacteria disappear from the blood within a few hours after the offending sinus has been excluded from the circulation. Schottmüller[4] as the result of observations on a great number of cases of septic abortion found that the enormous numbers of bacteria which enter the blood stream at the time of curettage in these cases (as demonstrated by blood cultures made simultaneously with the curettage) all disappear within a few minutes or at most an hour or two.

I have demonstrated the same point in cases of sinus thrombosis by counting the number of colonies per cubic centimeter of blood in the vein directly draining the infected sinus (one or the other internal jugular vein) and simultaneously in other peripheral veins and arteries.[5] There is

always a much larger number in the vessels directly draining the infected area; and careful mathematical studies demonstrated that the rate of removal of bacteria which were being fed into the blood was rapid.

### III. HOW ARE THE BACTERIA REMOVED?

Whole blood, citrated or defibrinated, can easily be shown to possess a very considerable bactericidal power for most varieties of pathogenic bacteria. From one half to nine-tenths of the bacteria added to blood, and in some instances, where very small numbers are added, all the bacteria added are killed within one hour's incubation.[6] Only a part of this effect is due to antibodies present in normal blood. A large part is due to the phagocytic action of leucocytes; and this is enormously stimulated by bactericidal antibodies when such are present.

However, the bactericidal effect of blood is a relatively slow matter. The removal of bacteria in disease is a matter of minutes. Recent studies of the phagocyting effect of the reticulo-endothelial system give us the rapidly acting mechanism needed to explain this. It is now known definitely that bacteria are removed by phagocytic cells in the capillaries of the lungs, liver, bone marrow, spleen and lymph nodes. Certain of these sites play a larger role in some and certain in other types of infections.

The presence of either normal or immune antibodies in the blood greatly accelerates the rate of removal of bacteria by the endothelial phagocytes in the various organs. This is demonstrated in Bull's experiments[7] with pneumococcus and typhoid bacilli injected into the circulation of rabbits and by Manwaring's experiments[8] with the liver of the dog. This explains why in so many diseases, such as meningitis, typhoid fever, pneumonia, etc., there is an initial temporary bacteremia, which disappears as soon as the defenses of the body are mobilized, but which in certain instances reappears later if these defenses become insufficient.

### IV. WHAT BECOMES OF THE BACTERIA WHICH DISAPPEAR FROM THE BLOOD IN ALL CASES OF BACTEREMIA?

A certain number of bacteria are believed to be excreted. Some organisms, for example the Staphylococcus aureus, less frequently the hemolytic and the non-hemolytic streptococcus, are sometimes found in huge numbers in the urine. Many organisms, as the typhoid bacillus, are found in large numbers in the bile; ultimately they leave the body by way of the intestinal canal. But the majority must be digested within the phagocytic cells. It is generally believed that the chill and the toxic symptoms of general invasions are due rather to endotoxins liberated from the dissolved bodies of bacteria than to the direct products of bacterial metabolism. This was suggested especially by the work of Römer, who found that usually a chill does not occur at the time the largest number of bacteria are found in the blood stream, but that on the contrary, the largest number of bacteria are often found an hour or two before the chill, and there is progressive diminution of the number up to and immediately after the chill. Actually after the chill the blood may be temporarily sterile.

In work done with Dr. Harry Weiss in which we counted the number of bacteria in the blood of cases of bacterial endocarditis from hour to hour we were able to establish the same kind of parallelism.[9] The maximum number of bacteria was not found at the height of the daily temperature but generally an hour or two hours earlier. At the time of the highest temperature the number of bacteria was often the smallest in the twenty-four hours. This is important not only from the theoretical point of view of the mechanism of fever production, but from the practical point of view. Taking blood cultures when the temperature is at its maximum, or as is common, immediately after chills is not necessarily the best procedure. Rather, if from the temperature curve one can approximately

anticipate the beginning of the temperature rise this is the optimal time to make the blood culture.

### V. How dangerous is the entrance of bacteria into the blood?

Until recent times it was thought that the mere entrance of bacteria into the blood was a relatively rare phenomenon and that the consequences were always very serious. We now know that neither of these statements is strictly true. There are many reasons for believing that bacteria in considerable numbers enter the blood on many occasions only to be removed rapidly without any further sequelae. Transient bacteremia at the time of operations on infected areas has been recognized for years. Schottmüller[10] showed that if blood cultures are taken at once after an opening is made into an ordinary local infected focus, especially if the infected focus has been under pressure (in a phlegmon or a closed organ, such as gall bladder or urinary bladder), it is not uncommon to find bacteria in the blood. It is rare, however, for this to be followed by the development of metastatic foci. Indeed we know that of the myriads of microorganisms which enter the blood in the diseases which we are discussing only a few ever do form metastatic foci. The great majority are removed without ever leaving any trace. Also numerous studies of recent years on the bacterial flora of the portal blood and the liver have shown that the entrance of bacteria into the portal blood from the intestines is probably not the exception but the daily occurrence. The enormous phagocytic power of the Kupffer cells which line the liver sinuses securely removes all of these bacteria so that for practical purposes the peripheral circulating blood is sterile. It is extremely probable that in many local infections a few bacteria enter the blood stream from time to time, but that for technical reasons we seldom detect them, and for the reasons noted they seldom give subsequent trouble. In such diseases as pneumonia the percentage of positive blood cultures that one obtains depends to a considerable extent on the amount of blood which one takes for culture. If one takes only a few cubic centimeters the occasional microorganism may escape detection. If one takes larger amounts of blood and especially if one uses large amounts of fluid culture media (in which isolated organisms grow out much more readily) one can get a much higher percentage of positive cultures. Even in diseases with obvious blood-borne metastases, the bacteremia is often intermittent; it occurs in "showers" as Walton Martin[11] well says. Whether one makes the blood culture at the right or the wrong moment is entirely a matter of luck. This is the reason that blood cultures, if at first negative, must always be repeated.

### VI. Diagnosis by blood culture

The diagnostic use of blood cultures might be discussed under three headings:

(1) The diseases in which the findings of a positive blood culture or failure to find it is frequently of direct diagnostic help;

(2) The inferences as to the probable location of the distributing focus that can be drawn from finding certain species of bacteria in the blood;

(3) The inferences that may be justifiable from the failure to find bacteria in the blood in the presence of certain clinical pictures.

There is an important group of long-continued fevers in which blood cultures are of the greatest differential value. If persistently used they are usually positive and diagnostic. These diseases are:

Subacute bacterial endocarditis
Chronic meningococcemia
Undulant fever
Typhoid and paratyphoid fevers
Gonococcal endocarditis
Infections with staphylococci and hemolytic streptococci.

In certain fevers ordinary blood cultures are commonly negative or if bacteria occur they do so transiently and are not regarded as of etiological significance. These are:

Rheumatic fever
Chronic infectious arthritis
Miliary tuberculosis
Atypical verucous endocarditis (Libman-Sacks)
Disseminated lupus erythematosus
Infectious mononucleosis

### VII. FEVERS WITH POSITIVE BLOOD CULTURES

While most cases of subacute bacterial endocarditis are due to non-hemolytic streptococci of the green-producing variety (viridans) occasional typical cases are caused by other organisms such as other non-hemolytic streptococci, for instance the enterococcus (a heat-resistant non-hemolytic streptococcus normal in the intestinal tract), the influenza bacillus or even the Staphylococcus albus.

I have seen one case due to Staphylococcus albus, a patient of Dr. Baehr. It differed from the usual clinical case in that the onset immediately followed a clean gynecological laparotomy complicated however by a superficial collection of serum in the wound: the serum yielded a culture of Staphylococcus albus. After a febrile course of several months, during part of which there was high spiking fever, white-centered petechiae and as many as 400 to 600 white staphylococci per cubic centimeter of blood the patient made a complete recovery and has remained well now for three years.

Chronic meningococcemia closely simulates subacute bacterial endocarditis. It can often be suspected, if not diagnosed, clinically. The disease is characterized by prolonged low-grade irregular fever, usually lasting for many months, by mild arthritic manifestations and by skin eruptions, usually scanty but at times abundant, appearing in crops most commonly suggestive of rose spots but varying from petechiae to slightly elevated erythema suggestive of erythema nodosum. Heart murmurs are common and it is possible that an endocarditis is the distributing focus for the meningococcemia, but this is not certain. Many patients get well. I have seen patients who recovered completely and left no evidence of valvular damage.

Recently I saw an autopsy on such a patient who died of a second attack of meningococcemia (this time of the fulminant variety) four years after recovery from his attack of chronic meningococcemia. This was a boy of fourteen whom I saw first over four years ago when he was a patient in the wards of Dr. Schick, suffering from a chronic meningococcemia from which he recovered completely. Some of the details are very interesting. His first illness in August, 1929 started suddenly with fever of about 103°F. every other day. His fever at that time was accompanied by shaking chills. After his admission this continued and he had six severe rises of temperature during his first two weeks in the hospital. At the same time he showed the characteristic rose-spot like eruption, accompanied, however, by occasional petechiae in the conjunctivae. Also he had a tender node resembling the typical Osler lesion on one of his soles. The spleen was just palpable, his white blood cell count was 28,000 with 90 per cent polynuclears. His blood culture was found to be positive for meningococcus. The numbers were very small for the culture was positive in the flasks only and the growth was very slow, requiring five days until the organism was definitely identified.

On the advice of Dr. Josephine Neil meningococcus serum was given intravenously in large amounts. Immediately following the use of the meningococcus serum the patient became afebrile and remained well during the month which he remained in the hospital. Repeated subsequent blood cultures were negative. He was watched in the clinic for a period of nine months and remained well for four years until his second admission in September, 1933.

Then he suddenly awoke with a chill lasting fifteen minutes, headache, nausea and vomiting. The following day he developed pain in all the joints and a profuse purpuric eruption over his entire body. When admitted to the hospital he appeared to be in shock; his temperature had been 106°F. before admission but was about 100°F. at the time of admission. He showed no neck rigidity, no Kernig sign. Smears from his purpuric lesions showed numerous intracellular meningococci and blood smears from a finger tip showed a few. The blood culture showed innumerable organisms. In spite of blood transfusions and intravenous meningococcus

serum, he died within twenty-four hours. Before he died he developed definite signs of meningitis.

At autopsy a careful search revealed no hidden focus which might have carried meningococci after the first attack. The heart valves were normal, indicating that if there had been an endocarditis during that attack of meningococcemia four years earlier, it must have healed without leaving a trace.[12]

The importance of recognition of chronic meningococcemia is twofold: (1) if unrecognized the disease runs on for months and may terminate in a meningitis; (2) most patients can be cured by intravenous use of antimeningococcus serum.

Another form of obscure fever which enters into differential diagnosis here is undulant fever (Malta fever), due to one of the bacteria of the Brucella group. In the case of Brucella militensis the infection is commonly from goat's milk products; with Brucella abortus it is from cow's milk or beef, with Brucella suis from pork products. The fever is one of very long duration, in some respects resembling that of chronic meningococcemia. It usually is relatively mild and the clinical symptoms which can lead to diagnosis are few. Recognition is most commonly accomplished by agglutination tests with the patient's serum; but often positive blood cultures can be obtained. A practical point is that the growth of the organism is slow so that if blood cultures are discarded in less than a week a positive result may be missed.

So-called "gonorrheal rheumatism" is most commonly a general infection due to transient bacteremia arising from some deep focus in the genital tract. This bacteremia commonly lasts for hours or days. In patients whose clinical features are at all suspicious, even if there is no local evidence of gonococcus infection, blood cultures should be made promptly. Sometimes this is the only way of definitely establishing the real nature of the infection. When blood cultures are persistently positive we are almost always dealing with gonococcal endocarditis. This shows the typical so-called "septic" type of temperature (extreme rises and falls accompanied by chills), and usually embolic lesions. It is a very fatal disease but occasionally patients recover spontaneously. I have seen one such recovery myself.

This was a woman of nineteen years who had had a curettage for abortion by a midwife three and a half months before. This was followed by daily fever for the whole period, the fever often reaching 105½°F. and being preceded by true chills. In the beginning she had suffered from some lower abdominal pain but this had rapidly subsided. She had had one blood transfusion before admission to the hospital. When seen she was very pale; hemoglobin 62 per cent. She showed one petechia in the conjunctiva. She had all the physical signs of an aortic insufficiency. Her blood pressure was low, systolic 94, diastolic 30. In spite of the low blood pressure she had the urinary findings of glomerulo-nephritis, with considerable amount of albumin and red blood cells, hyaline and granular casts in the urine. Her spleen was enlarged, coming down two fingers below the free border of the ribs. She did not show a total leucocytosis; polynuclears were 83 per cent. The leucocytes, however, did show marked toxic granulation (this is quite characteristic for severe infections).

Under observation she continued to run daily spiking fever with occasional chills. She developed one flame-shaped embolic hemorrhage over the dorsum of the foot. Her blood culture was positive for gonococci on two occasions but in the flasks only. In spite of repeated attempts it was never possible to detect gonococci in the cervix or urethra and the pelvic examination gave no evidence of active disease. Gonococcus fixation was positive (4 plus).

The interesting point about this patient was that after running this high temperature in the hospital for two weeks one day the temperature rose to 104.8°F. with a chill. Thereafter it dropped to subnormal, 97°F. and remained permanently normal, and blood cultures remained negative after this. Apparently there was a spontaneous cure.[13]

I may suggest that on account of the low heat resistance of the gonococcus which is known to be killed by a tempera-

ture of about 109°F. it is possible that the cure was effected by the high internal temperature at the time of the chill. This should be kept in mind in considering future therapy.

As already stated blood cultures are of the greatest usefulness for the diagnosis of typhoid fever in the earliest weeks at a time when the Widal reaction has not yet become positive. As a rule it is only during the early weeks or in the beginning relapses that one gets a positive blood culture, although occasionally in very severe cases blood cultures may also be found to be positive in the later weeks.

Next to this group of prolonged fevers, perhaps the greatest practical use of blood cultures is in so-called "otogenic sepsis." Here the rules laid down years ago as a result of the investigation of Libman and his co-workers[3] have only been confirmed by further experience. In these cases the finding in the blood of hemolytic streptococcus or of pneumococcus, type III (formerly called Streptococcus mucosus) almost invariably indicates the existence of a sinus thrombosis and is an urgent indication for operation. Very rarely a non-hemolytic streptococcus may be found. The absence of streptococcus from the blood does not rule out sinus thrombosis. The finding of pneumococci (other than type III) in the blood does not point to sinus thrombosis, but commonly to a complicating pneumonia. The finding of streptococci in the blood within a day or two after a mastoid operation, however, can not be regarded as conclusive especially if the number of organisms is small, because occasionally a postoperative bacteremia may last as long as this: in such a situation the blood culture should be repeated.

There are rare cases of general infection arising from the ear in which in spite of the finding of streptococci in the blood one may still be in doubt as to whether the source of the streptococci is a sinus thrombosis. The cases referred to are those in which symptoms suggestive of endocarditis, kidney suppuration or pneumonia lead one to suspect that some secondary distributing focus may be feeding streptococci into the blood. In this situation a "differential blood culture,"[14] a procedure which I introduced some five years ago, may occasionally be of assistance. The differential blood culture consists of three simultaneous cultures made by separate punctures of the two internal jugular veins (which directly drain the lateral sinuses) and an arm vein. The number of colonies per cubic centimeter in the blood from each source is carefully counted. A very great preponderance of numbers in either jugular vein indicates that the bacteria are coming from a lateral sinus. Unfortunately it is not possible to state from which lateral sinus, because the bacteria may be coming from either the lower or the upper end of the thrombus. The failure to find such a difference does not rule out lateral sinus disease. The finding of large and uniform numbers in all the sites usually indicates a complicating acute bacterial endocarditis as the cause of the bacteremia.

A situation in which blood cultures would be of diagnostic aid much more frequently if they were performed more often is the "septicemia of the newborn." Blood cultures are seldom done as a routine because it is generally considered that they are impractical. Actually with the use of a fine needle, blood cultures by the method of Marfan from the superior longitudinal sinus can be done with perfect safety. There are three chief forms of septicemia of the newborn: (1) icterus gravis, (2) melena or purpura, and (3) enteritis.

In the pre-bacteriological days there were a number of clinical pictures in the newborn described as separate diseases: thus, von Wickel's disease, a combination of hemoglobinuria and icterus, and Buhl's disease, a combination of purpura and fatty degeneration of various viscera. These diseases which formerly often occurred in epidemics, were probably various forms of general infection. Though the epidemics of former years no longer occur, I believe, from my own limited experience, that

septicemias of the newborn are more common than statistics indicate, and that some deaths assigned to other causes are really due to infection. It is characteristic of the new-born that their tissues seem to offer little resistance to bacterial invasion so that the local lesions at the point of entry (usually the umbilicus) are often inconspicuous while general intoxication and visceral degeneration dominate the picture. The typical fever curves, chills and embolic manifestations of adults are often missed. There may be actually hypothermia. Various kind of cutaneous hemorhages, and eruptions, such as pemphigus, may be important for diagnosis. The hemorrhagic diathesis is sometimes due to complete incoagulability of the blood.[15]

In pneumonia the chief use of blood cultures is as a guide in therapy and prognosis. On the average the cases which show positive blood cultures are graver. While there still remains in the minds of many physicians a doubt as to whether specific therapeutic serum is indicated in the milder cases which do not show microorganisms in the blood, there is no doubt that it is of use in the severer cases which have them. Aside from the clinical benefit reported in many large series of cases, this is shown by the prompt sterilization of the blood after the injection of the specific serum. Blood culture also is of value for obtaining the invading pneumococcus for type identification. A blood culture should be made as soon as a case is recognized as pneumonia. For blood cultures in pneumonia Bullowa recommends that a small amount, 3 c.c. of blood, is sufficient. It must, of course, be well diluted in fluid media.

### VIII. FEVERS WITH NEGATIVE BLOOD CULTURES

In the group which give negative blood cultures it should be stated that certain workers by special methods have described the finding of streptococci in the blood in rheumatic fever and in infectious arthritis. This is a controversial field which it is not necessary to enter here. For practical purposes in these diseases ordinary blood cultures are negative; if a positive blood culture is obtained some other condition is to be diagnosed, or at least the etiological relationship of the organism to the disease is at present open to question.

In the list which give negative blood cultures, I will refer briefly to two, namely, the atypical verucous endocarditis of Libman and Saks and disseminated lupus erythematosus. I do so because though these are very definite clinical entities they are not sufficiently well known and are often forgotten in the differential diagnosis of prolonged fevers.

Atypical verucous endocarditis[16] is a remarkable and well-characterized disease which should be recognized clinically. In some ways it resembles subacute bacterial endocarditis, but blood cultures (and cultures from the heart valves at post mortem) are negative, and the causative agent is unknown. The disease runs a subacute febrile course with anemia, leucopenia, erythematous eruptions, occasional white-centered petechiae and necrotic lesions of the mucous membranes. Pneumonia, pleurisy, pericarditis, arthritis, glomerulonephritis often develop in its course. In all the cases recognized so far the patients have died.

Closely similar, so closely similar in fact that there is doubt whether it is not another form of the same disease,[17] is disseminated lupus erythematosus which, since Kaposi described it in 1872, has been recognized by dermatologists as a unique disease. Its kaleidoscopic picture includes most of the features just described for atypical verucous endocarditis except the endocarditis (but there may be a terminal verucous endocarditis) and perhaps the petechiae. The eruption (which may be absent for long periods) differs greatly from the common chronic discoid lupus erythematosus and is often more like erythema multiforme.[18] In fact ordinary lupus erythematous has little in common with this disease except the "bat-wing" distribution on the face.

The prognosis is extremely bad. It is difficult to find a record of any case in which the patient undoubtedly had this disease and recovered.

A particularly interesting case of this disease was seen by me last June. It was a young woman of twenty-three who was said to have had rheumatic endocarditis at the age of ten but who had never had any further sickness. Six months before, she had developed a "grippe" followed by a red, blotchy eruption, first on the face and then on the entire body. This gradually cleared up in the course of about one month and a half but was followed by a bout of arthritis in various joints which kept her in bed for about two weeks. Then she was well until about two weeks before. She then began to run daily fever up to 103°F. At the same time a dusky red eruption developed all over the body. She was quite pale, with a hemoglobin of 55 per cent. She had an erythematous bluish eruption without scaling or atrophy over the bridge of the nose and the adjacent areas in the cheeks, forehead, temples and scattered over the trunk, especially marked over the elbows. Her pulse was 130, her temperature 105°F. She had no leucocytosis. Mantoux tuberculin test was negative. There was a considerable amount of albumin with hyaline and granular casts in the urine. Blood chemistry remained normal. The patient finally developed signs of bronchial pneumonia. Repeated blood cultures were negative.

During the second week the skin lesions became more profuse, forming large circular lesions on the trunk. The day before death, which was two weeks after she was first seen, she developed a pericardial friction rub. A post-mortem examination was made and showed very extensive hemorrhagic bronchial pneumonia, and fibrinous pericarditis. There were no endocardial lesions such as are seen in the cases of atypical verucous endocarditis described by Libman and Sacks. On microscopic examination the kidneys and other organs showed vascular lesions considered by Dr. Klemperer as characteristic of disseminated lupus erythematosus.

The whole subject of the significance of persistently negative blood cultures in fevers is of great importance. Libman[19] has written extensively on this subject and what I shall say I learned from him.

There are many conditions which simulate general bacterial invasion but in which the failure to find bacteria in the blood may help to the right diagnosis. Some of these are conditions in which bacteria possibly occur in the blood but in which our methods are inadequate to find them. Some are local infections in which, a priori, one might expect to find bacteria in the blood but in which experience shows the blood is seldom invaded.

Among conditions which may simulate general bacterial infections, other than the continued fevers already discussed, are Hodgkin's disease (the so-called "Ebstein" type of fever), leucemia and breaking-down new growths.

Of the severe local infections in which the absence of bacteremia is striking the most important from the diagnostic point of view is pylephlebitis, due usually to an antecedent unrecognized appendicitis or other abdominal infection. High irregular fever with chills, but with no peripheral metastases, and with persistently negative blood cultures should cause suspicion of suppurative inflammation of the portal vein. In over 40 cases Libman found organisms in the blood only 3 times and then only shortly ante-mortem. This is probably due to the great phagocytic power of the cells lining the blood sinuses of the liver. Occasionally it may be due to the fact that the invading organism is an anaerobe not detected by the usual method of blood culture. For the same reason liver abscess and cholecystitis rarely cause blood infection (unless there is also a cholangitis which not infrequently does cause blood invasion).

Other severe conditions in which bacteremia rarely occurs are empyema, breast abscesses, appendicitis, peritonitis secondary to intestinal diseases (as compared with peritonitis due to pneumococci or streptococci in which blood cultures often are positive) and secondary parotitis consequent to the mouth infection of very ill patients or following abdominal operations.

IX. SEARCH FOR THE DISTRIBUTING FOCUS

In the study and treatment of bloodstream invasions it is important to distinguish between:

(1) The portal of entry, which does not necessarily remain permanently a point of distribution;

(2) The focus of distribution, adjacent to or within the vascular stream;

(3) Metastatic foci, most of which, as Libman's studies show, seldom act as distributing centers for the blood stream.

It is often extraordinary to what extent recovery can take place from secondary, or metastatic foci due to the streptococcus, staphylococcus, pneumococcus or gonococcus, provided the distributing focus is removed. From the practical and especially from the surgical point of view, therefore, it is the discovery and treatment of the distributing focus which is important.

In obscure fever cases whether metastatic foci are found or not, the finding of either Staphylococcus aureus or hemolytic streptococcus in the blood is of the greatest importance. It always means that there exists at least one focus which is feeding the organisms into the blood. It is the duty of the physician to find this focus and to remove it if that is possible. In most cases this offers the only hope for the patient. With staphylococcus one asks particularly for the history of an antecedent furuncle and one looks especially for a hidden distributing focus in the form of osteomyelitis, prostatitis, seminal vesiculitis or kidney suppuration.

When the hemolytic streptococcus is found in the blood the initial point of entrance is more likely to be tonsils, ears, uterus, or small wounds and abrasions; and one has to look particularly for evidence of thrombophlebitis in the region adjacent to the point of entry. The search for the offending distributing focus in an obscure case (which until such a focus is found can justly be called by the old term "cryptogenetic sepsis"), is one of the most exciting and difficult procedures in the practice of medicine. Every obscure and hidden cranny of the body has to be carefully investigated. The aid of various specialists, such as gynecologists, otolaryngologists, etc., has to be enlisted and all the resources of clinic and laboratory have to be called in.

One often forgotten location in which I have twice discovered such a focus is a deep axillary gland. Both cases were due to hemolytic streptococci. In the first of these 2 cases the only antecedent history was of a throat infection some days before the onset. In the other case a small blister on the finger a week or two prior to the onset had probably lead to the infection of the axillary node. In both cases there were no complaints pointing to the small focus of deep suppuration and it was only on going over the patient carefully that tenderness and deep lying induration were noticed under the upper part of the pectoral muscle. Operation in both cases showed suppuration at the very apex of the axilla. In the second of the 2 cases this had produced an extensive phlebitis of the axillary vein. Both patients ultimately recovered after operations (performed by Dr. Neuhof).

If, after proper surgical attention to the assumed distributing focus, the bacteremia continues, further search for other distributing foci must be very thorough, and every such possible focus must be operated on in a most radical manner. Both the staphylococcus and the hemolytic streptococcus produce suppurative metastases in many parts of the body, and the most important function of the physician is to recognize and to treat each of them.

The staphylococcus has a far greater tendency to produce metastases than the hemolytic streptococcus and this is the reason on the whole that it is the more dangerous and fatal. Especially it produces multiple abscesses (so-called "furuncles") of the lungs and of the kidneys, which on account of their numbers as well as their inaccessibility are usually not open to surgical treatment. Nevertheless treatment

must never be regarded as hopeless and an occasional patient even with multiple lung foci does recover. The almost invariably fatal metastases due to the streptococcus, staphylococcus and pneumococcus are meningitis, peritonitis and acute bacterial endocarditis.

Metastases from the hemolytic streptococcus can occur, like those of the staphylococcus almost anywhere. One has to watch particularly bone marrow, joints, and tendon sheaths. While it is true that the body often can and does take care of arthritis, periarthritis, synovitis, or adenitis, and that usually these lesions do not directly feed the blood stream, nevertheless, if the infection persists an attempt should be made to eradicate by surgical means every metastatic focus. The mistakes I have seen made have almost always been on the side of conservatism rather than radicalism. When a local focus is explored it is vital that a search be made for an infected vein as it is there above everything else that the distributing focus is likely to be found.

In postpartum and postabortum infections, blood cultures are of some aid. Of the aerobes the most common organism found is the hemolytic streptococcus. Occasionally the Staphylococcus aureus, non-hemolytic streptococcus or the Bacillus coli are found. Schottmüller's work showed that anerobic blood cultures must invariably be used in this field; he recognized that the anerobic Streptococcus foetidus (of Veillon—renamed "putridus" by Schottmüller) and also a peculiar anaerobic staphylococcus, as well as the Welch bacillus are frequent blood invaders. There are many other anaerobic organisms which may occur. The whole subject of anaerobic blood bacteriology is somewhat in its infancy. While the finding of organisms in the blood stream in these cases does not necessarily lead to any different plan of treatment of the portal of entry than that which would be adopted if the organisms were not found, it accentuates the importance of persistent watchfulness for metastatic foci. The anaerobes especially tend to produce metastatic lung foci.

There are one or two organisms which are more rarely found in the blood but the finding of which is sometimes of special significance as pointing to the focus of entry. Thus the Friedlander bacillus (Bacillus pneumoniae) most commonly enters the blood stream by way of infected bile ducts. It may also be found in the blood in cases of primary Friedlander bacillus pneumonia, and in infections of the urinary or intestinal tracts.

Other organisms which can cause a general infection starting from the gall bladder or bile ducts are the Bacterium coli and various anaerobes, particularly the bacillus of Welch.

### X. THERAPY OF BACTEREMIAS

The surgical treatment of bacterial invasion of the blood, where it is possible, is the most important. Attention has to be centered not on the primary portal of entry so much as on the distributing focus. Constant watchfulness for new surgically accessible metastases has to be maintained.

The medical treatment is essentially supportive. In only a few bacteremias, such as for example those caused by pneumococcus or meningococcus, is serum therapy helpful. Serum may be tried in gonococcus blood stream invasions but the results have not been very favorable. In streptococcus and staphylococcus infections the sera so far available have been ineffective.

The same unfortunately must be said of chemotherapy. None of the large list of the bactericidal drugs, including mercurochrome, acriflavine, optochin, gentian violet, is of any use against generalized infection. In experiments which I have performed with these and other drugs I have found that they lose nearly all of their effectiveness when mixed with blood. In practice it has been found that it is impossible without the severest toxic effects to introduce enough of any of these drugs to cause the killing of bacteria in the blood or tissues. While the search for chemo-

therapeutic substances is still going on unceasingly, and undoubtedly will ultimately be successful, it must be acknowledged that at present there is no chemotherapy of general infections.

This does not mean, however, that there is not much for the physician to do. In fact the bolstering up of the patient's general condition is the most important part of the treatment. The sufficient administration of food and fluids, and detoxication by intravenous glucose injections are very important.

The use of blood transfusion plays a large role. It must be regarded as one of the general supportive measures rather than having a specific role. In acute fulminant "sepsis" it is seldom successful. In prolonged infections where the body has already demonstrated that it is able to put up a stiff resistance to the invader persistent blood transfusion sometimes gives just the added strength needed. Of the various methods of transfusion I believe that the citrate method is to be preferred because of its ease. The advantages which were formerly claimed for one or the other of the syringe methods are theoretical rather than real.

The use of immunized donors is unfortunately in most cases impractical both on account of the expense and the time necessary to prepare such donors. For this reason no one has as yet been able to put it to extensive enough test to learn whether it has any actual advantages. The so-called "immuno-transfusion" which has been advocated by Wright[20] is somewhat different in principle. An intravenous injection of a not necessarily specific vaccine is given to the donor five hours before the intended transfusion; then at the time when his post-injection reaction has reached its climax, and when his blood is supposed to have mobilized the defensive elements of his system, blood is transfused from him. While experimental justification for this method is not entirely satisfactory, it deserves a trial not as yet received.

Transfusion should be used with persistence. The attempt to replace most of the patient's blood at one sitting, the so-called "exsanguination transfusion" of Robertson,[21] is seldom feasible except in small children. Its possible benefits are well brought out by the results in the highly fatal erysipelas of infants (in which bacteremia is the rule): of 33 cases not transfused 18 died, of 16 transfused 15 recovered.[22]

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# SURGICAL CONDITIONS OF THE KNEE JOINT*

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THE subject for consideration in this paper, the knee joint, was deliberately chosen by me because surgery of the knee joint was advanced, one might almost say popularized, by the man in whose honor this annual lecture is given, Sir Robert Jones. This is the first year since the founding of this lectureship that the lecturer has not felt that across the ocean there still lived this keen, astute, able, kindly man who did more to develop orthopedic surgery and place it in the honorable position it now occupies than any other man living or dead. To a certain few of us here tonight his is a real personality that stands out vividly in our memories, because we knew him and looked on him as our teacher and friend. As a young man it was my privilege to spend two, never to be forgotten, fruitful months with him at his workshop, 11 Nelson Street, in Liverpool, where I came under the spell of his magnetic and genial personality. I cannot let this occasion pass without a brief review of his life and accomplishments, although it can be but a sketch.

Sir Robert Jones died on January 14, 1933 in his seventy-fifth year. He died as he would have wished, in harness, and there were only a few months toward the last during which he was not able to carry on with his accustomed vigor. He was born in Rhyl, in North Wales, on June 28, 1858. One cannot consider the life of this man without mentioning also his uncle, Hugh Owen Thomas of Liverpool, because of the intimate association of the two, Jones as the pupil and Thomas as the preceptor. Thomas was descended from a long line of unqualified bone-setters, but he graduated in medicine and established a large practice in Liverpool, drawing patients from far and near. He was a general practitioner but was also an orthopedic surgeon. Robert Jones came into the practice of this remarkable man in 1878. He proved himself a receptive pupil, and early demonstrated exceptional intellectual and physical vigor. He soon was appointed on the Staff of the Royal Southern Hospital, where he founded the orthopedic clinic which later became world-famous. His surgical activities were at first in the entire domain of surgery, but it was not long before he was forced to restrict his field to the domain of orthopedic surgery.

Although his work was well known to a small group of orthopedic surgeons in America, it was not until 1907 that American surgeons as a whole became cognizant of what was going on in Liverpool. William J. Mayo, on returning from a trip abroad stated:

> Just as Lawson Tait carried sound surgery into the abdomen, and Mr. Victor Horsley into the cranial cavity, so has Mr. Jones carried sound surgical principles into orthopaedic practice, and rapid cures are the result in a large number of cases in which treatment had been given for months and years by orthopaedic apparatus. This does not mean that Mr. Jones has discarded these measures. He is most careful in the after treatment and uses mechanical contrivances for their proper purposes as an adjunct to surgery, not in place of it. All operations are done under ether anesthesia. The asepsis is most painstaking and thorough. He is expeditious, yet neglects not the smallest detail and his wonderful experience enables him to do wizard-like operations with a precision that is startling. So unassuming and modest is the man that he is, I believe, entirely unaware of his great ability.

* The fourth Sir Robert Jones Lecture to be delivered at the Hospital for Joint Diseases, New York.

When the World War broke out in 1914, and British hospitals were filled to overflowing with the injured sent home from France, Sir Robert was the man who took charge and met the situation. It was during this time that he came to be really appreciated in England, and rose to his full stature. He was appointed director of military orthopedics and later he was made Major-General in the British Army Medical Service. Ultimately he had under his supervision more than 30,000 beds. When the war was over, he received every honor that could possibly fall to a surgical leader. It was not until after the war that he was able to carry through to completion the project long close to his heart, the establishment of a system of orthopedic hospitals such as are now to be seen in Aberdeenshire, Lancashire, Manchester, Birmingham, Alton, London, and so forth. In this early work, a remarkably able woman, Dame Agnes Hunt, a former patient who had become fired with the desire to help the crippled, was associated with Sir Robert, and this association was carried on down through the years until his death.

Therefore, we see that there are three periods in the life of Sir Robert Jones which stand out: (1) the period in Liverpool when he established the large clinic and made his reputation; (2) the period of the war, when he rendered incalculable benefits to the wounded through his ability for organization and for teaching of sound, practical principles to great numbers of other surgeons; (3) the post-war period, which corresponded with the later years of his life, but during which his physical vigor and intellectual keenness were undiminished.

The personality of the man was outstanding and delightful. Lord Moynihan wrote in the preface to the Jones birthday volume:

> Few men have ever possessed in so radiant a degree the genius for friendship. No one can be long in his company, none can work with him or play with him, without realizing not only the sweet simplicity of his character, but the greatness of his heart. . . . In a long and very intimate friendship I have never heard an unjust criticism, a cruel gibe, or a word of bitter cynicism on his lips. His personality radiates cheerfulness, good temper and good will.

## ANATOMY OF THE KNEE JOINT

The knee joint is the largest joint of the body, and is the most superficially placed. It is a modified hinge joint, in which the articular surfaces of the bones are not closely adapted to one another, and in which there is never more than a small area of the femur in contact with the tibia in any position of the joint. This permits a slight degree of sliding and rotation to take place in addition to the hinge movement.

The strength of the joint is dependent on the integrity of the crucial ligaments and of the extrinsic ligaments and muscles. Concerning these structures I shall mention only one or two facts. The internal lateral ligament is of great importance, and is firmly attached to the internal semilunar cartilage. The semilunar cartilages are crescentic disks, wedge-shaped in transverse section, and each cartilage assists the opposite lateral ligament in resisting lateral movements of the leg. The semilunar bodies consist of a core of fibrous tissue arranged transversely and longitudinally. Although the knee joint is the most superficial of all joints, and is covered laterally only by skin and capsule, and anteriorly only by these and the patella, the fact that the joint depends for its stability on the integrity of its ligaments, renders free exploration of its cavity difficult, and necessitates carefully planned incisions for exposure if the stability of the joint is to be maintained with motion.

## LESIONS TO BE CONSIDERED

I shall confine my consideration of the knee joint to four surgical conditions. The first two are non-traumatic, namely, tuberculosis and arthritis; the last two are traumatic, namely, lesions of the semilunar

cartilages and recurring dislocations of the patella.

### TUBERCULOSIS OF THE KNEE

In onset, tuberculosis of the knee joint may be sudden or insidious; usually it is the latter. It is always secondary to a focus elsewhere in the body; the infection reaches the knee by way of the blood stream, an extremely important fact to remember in treatment. I intend to present to you briefly a résumé of a study that we recently made at The Mayo Clinic, of all cases in which resection of the knee joint has been performed up to the present time. However, I do not feel free to embark on a discussion of the surgical phase of the treatment without at least mentioning the non-operative treatment, often erroneously called the conservative treatment. The most conservative treatment may, as a matter of fact, be surgical treatment. There is no doubt that by rest, fixation, and tonic measures a certain percentage of patients with tuberculous knees can be carried through to cure, to arrest of the disease, or to ankylosis. Long confinement under strict supervision in an orthopedic hospital is necessary, however, and in this country a sufficient number of beds in such hospitals is not available. Inasmuch as most orthopedic surgeons seem more than satisfied if a patient can be cured of a tuberculous knee joint by ankylosis, I see no reason why, other things being equal, tuberculosis of the knee joint should not be treated by resection or arthrodesis. This has long been the practice in The Mayo Clinic, and our results have justified the practice. In the majority of the cases which we encounter, it would be utterly impossible to carry out prolonged non-operative treatment. The patients come from long distances, and often live far from any center where orthopedic care can be provided, particularly for adults.

*Source of Infection.* Tuberculosis of the joints is on the decline. No doubt the Mycobacterium tuberculosis (bovis) frequently has been responsible for tuberculosis of joints, and certification of herds and pasteurization of milk has done much to reduce the incidence of the disease. The avenue of entrance is either through the intestinal tract, into the mesenteric lymph nodes, or through the lungs into the bronchial lymph nodes.

*Consideration of Cases.* In 1927, before the American Orthopedic Association, I reported on 211 cases of tuberculosis of the knee joint in which arthrodesis was performed between 1913 and 1926. From 1927 to date we have operated in 63 additional cases, making 274 in all. Two-thirds of the patients were males. Trauma seemed to have something to do with the development of the lesion in approximately 13 per cent of the cases. In 44 per cent of the cases we were able to demonstrate tuberculous foci elsewhere than in the knee; the most common site was the lungs. A family history of tuberculosis was obtained in about 8 per cent of the cases.

*Symptoms and Diagnosis.* The outstanding subjective symptoms of tuberculosis of the knee joint are stiffness and pain, whereas the objective symptoms are local warmth, deformity and limping. The disease is characterized by chronicity with remissions, but the patients are never completely free from symptoms. When erosion of the joint has occurred, the pain may be excruciating and may be elicited by jarring or jolting. Thickening of the capsule is commonly seen, but effusion within a thin capsule is rarely seen. Naturally, in the vast majority of a group of cases such as these, in which resection was done, a clinical diagnosis of tuberculosis could be made. All cases in our series were proved to be examples of tuberculosis, either by pathologic examination of the tissue or by inoculation of guinea pigs, or both.

*Pathology.* It is not possible to state in any given case whether the disease is primary in the synovia or in the bone. In approximately 9 per cent of our cases the bone did not appear to be involved and,

therefore, we concluded that the synovia was the primary site. We found abscesses in the bone at the time of operation in approximately 50 per cent of the cases. Sequestra were present in 11.1 per cent of the cases.

*Differential Diagnosis.* Chronic infectious arthritis is more common than is tuberculosis of joints, and often, in the former condition, many joints are involved. Erosion of bone, as evidenced in the roentgenogram, is rarely as extensive in chronic infectious arthritis as in tuberculosis. In gonorrhea a history of primary infection usually can be elicited and the initial symptoms are acute. At first other joints are involved, the disease finally settling in one joint. Syphilis, in our experience, rarely affects the knee joint, but it may produce a confusing picture. The blood tests are almost certain to be positive if the lesion is due to syphilis. In hemophilia a positive family history may be obtained and suspicious changes in the blood, such as increased coagulation time, should be considered.

*Treatment.* Arthrodesis by resection is the operation of choice, but it should not be performed when draining sinuses are present, when patients are very young or are old, or when patients are debilitated by disease and their expectancy of life is short. We have rarely done the operation on patients who were less than nine years of age. If any of the vital organs are affected by tuberculosis, they should receive attention first; for example, if a single kidney is involved, the kidney should be removed first and the knee treated later. Even if the tuberculous involvement is general, if patients have a fair expectancy of life, and a great deal of pain in the knee, resection, I believe, is preferable to amputation. A few of our patients, whom we knew had disseminated tuberculosis and were doomed to die of it, lived anywhere from a year to five years in comfort with a stiff knee.

It should be borne in mind that arthrodesis of a tuberculous joint is performed to obliterate motion and, whenever possible, as much of the tuberculous material as can be reached should be removed at the same time. It has been our experience that as removal of the tuberculous material is the more nearly complete, so will the fusion be quicker and the likelihood of subsequent development of abscess be less. The complete and radical type of excision, which we have finally adopted in our work, has been followed by a materially reduced incidence of that type of abscess which is known occasionally to follow arthrodesis of tuberculous joints, perhaps years later.

*Technique of Operation.* On the day before the operation the hair is shaved from the leg, both above and below the knee, and a dry dressing is applied. Actual preparation of the region of the operation is made when the patient is on the operating table. Then, from groin to ankle, the leg is cleansed with benzine and ether and next, several coats of iodine or merthiolate are applied. Stockinet long enough to reach from ankle to groin is slipped over the foot and is left rolled at the ankle. The foot and leg are wrapped in a towel as far as the upper third of the leg, and the wrapping is held in place either by a bandage or rubber bands. The leg is elevated to deplete it of blood and a tourniquet is applied, over a folded towel, at the middle third of the thigh.

A transverse cutaneous incision is made across the front of the knee joint, just below the patella, and is extended about two-thirds the way around the leg. The skin is lifted up far enough to expose the patella and is retracted down far enough to expose the upper end of the tibia. The joint is opened by a transverse incision across the joint-line, severing the patellar ligament. The incision is carried far enough back on either side to permit acute flexion of the knee on the thigh. The patella is dissected upward, removed, and kept sterile in case it should be wanted for use as a graft.

The suprapatellar pouch, and the synovia at the margins, are thoroughly removed.

An incision is made through the soft tissues that embrace the upper end of the tibia, so that the saw can be introduced; enough of the upper end of the bone is removed to expose fully the cancellous structure. If abscesses are found in the bone they are thoroughly curetted, the membrane lining then is removed, and the cavity is swabbed with iodine. Care is taken to saw off, squarely, the upper end of the tibia. The saw is then introduced into the femoral condyles; no great care is taken to have the angle accurate, because later enough bone is removed to provide the proper angle.

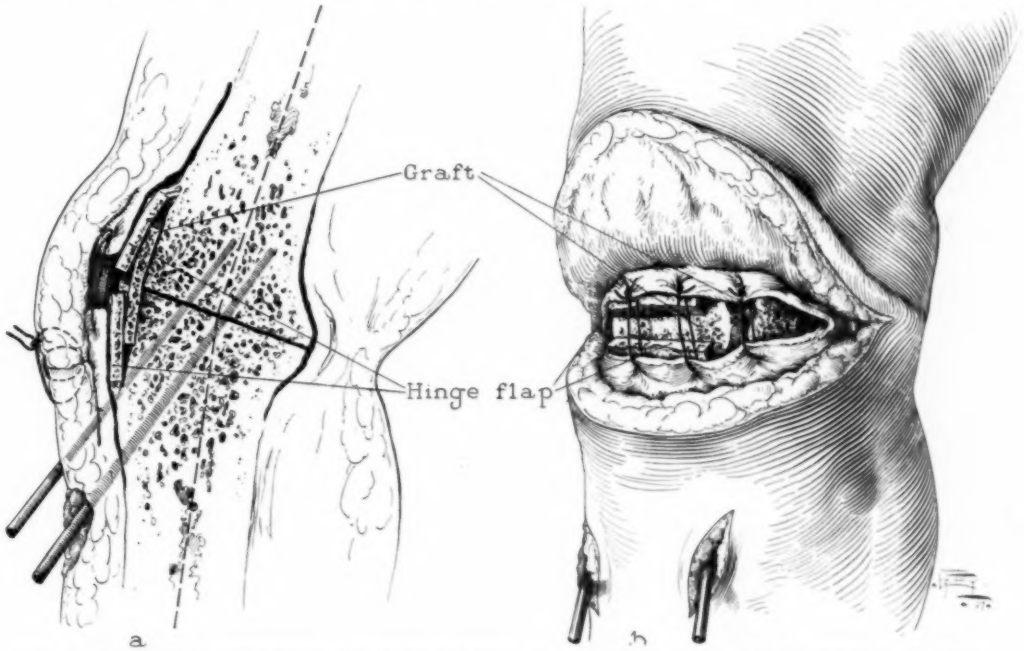


Fig. 1. Arthrodesis completed. Surfaces coapted, wire nails in situ and bone graft in position.

The knee is still held fully flexed and the upper end of the tibia is pulled forward, thus exposing the posterior capsule, which is dissected out. We believe that it is essential to remove as much as possible of the affected tissue. More bone is then removed from the femoral condyles, the amount depending on the angle of election for the arthrodesis, usually 10 degrees of flexion. This piece of bone is excellent for a graft, as it is cancellous and rich in bone-forming properties. It is carefully kept warm in hot saline packs. Two small, vertical incisions are made in the leg, one on each side of the median line, about 12 cm. below the upper end of the tibia; these incisions are carried down to the bone. Two wire nails are driven, in a slanting direction, through these incisions, upward into the tibia, until their points can just be seen beneath the surface of the bone. The chisel is driven vertically down along the anterior margin of the upper end of the tibia, and the tissues, with a good sized leaf of bone, are pried outward, making a trough about 2 cm. deep. If enough of the prominence of the condylar area of the femur remains anteriorly, the same procedure can be carried out on the femur, but often this prominence is lacking.

All is now ready for the coaptation of the ends of bone at the desired angle. The ends are brought together and held firmly while the wire nails are driven through into the femur. The proximal ends of the nails are left protruding through the skin. The graft is then removed from the saline pack in which it has been wrapped and is pushed down in the trough prepared for it in the tibia; thus it has bony contact on two sides. It can be molded somewhat, as it will bend considerably without fracturing. If a flap has been secured on the femur the graft is tucked within the

resulting crevice (Fig. 1). If there is no such crevice, the graft is molded to the femur and held in place by catgut sutures

new dressing placed within it. The leg is replaced at the same angle as before and the wire nails are removed. The nails come

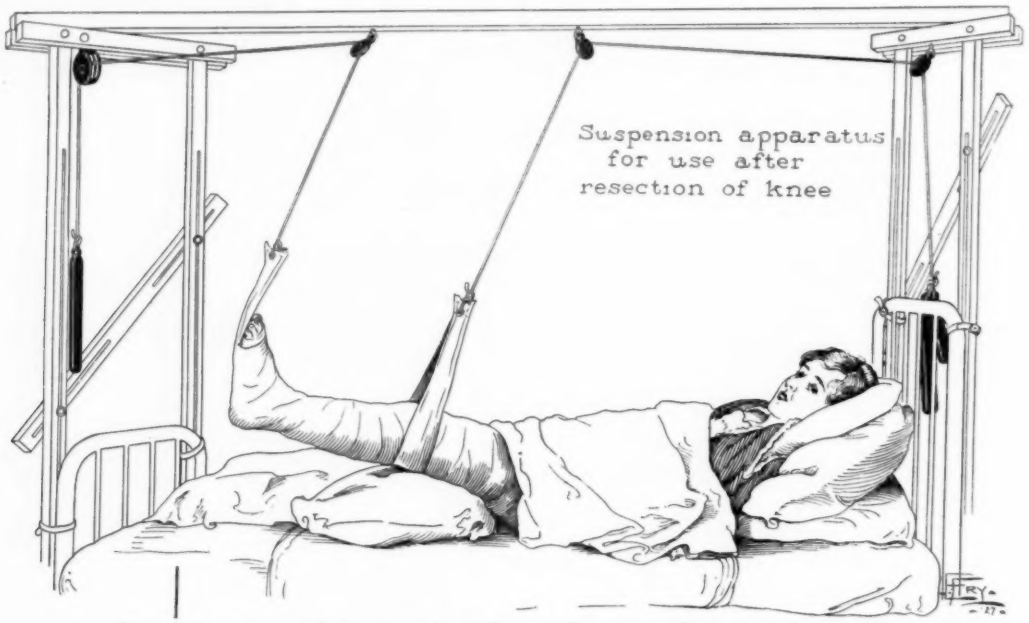


Fig. 2. Leg suspended to overhead frame. Cast extends from toes to groin.

extending from the soft tissues of the femur to the soft tissues of the tibia. The remnants of the capsule are brought together as completely as possible and the skin is closed. The leg is held vertically, care being taken to maintain the desired angle of flexion, and a thick dressing is applied firmly. The tourniquet is then removed.

The stockinet, which was previously applied to the foot and rolled at the ankle, is rolled up the leg to the groin, and eider-down bandages are bound about the leg for padding. A plaster-of-Paris cast is then applied, extending from the toes to the groin. Canvas strips for suspension are incorporated in the cast at the foot and knee.

The patient is put in bed and the leg suspended to an overhead frame so that the leg is free of the bed and the suspenders tend to force the lower fragment against the upper (Fig. 2).

Suspension is maintained for three weeks, at the end of which time the ventral half of the split cast is removed, the leg carefully lifted out, the stitches removed, the bottom half of the cast cleansed, and a

out easily at this time and cause little or no pain on withdrawal. A clean dressing is applied to the knee, and a few wraps of plaster bandage are put around the old cast. About ten days after this the patient is allowed to be up in a wheel-chair, and perhaps to stand with crutches. Six weeks after the operation, a new cast, which is lighter than the old one, and which has shoulder straps to relieve the weight on the leg, is applied, and the patient is allowed to go home with crutches with instructions to return in three or four months for examination and change of cast or for fitting of a brace.

*Operative Mortality.* No deaths that could be attributed to the operation occurred in our series of cases.

*End-results.* The end-results in a previously reported series of 211 cases showed that 17 (8.7 per cent) of the patients had died, but even these had lived an average of four and a half years following operation. These deaths were chiefly due to tuberculosis extending to other organs of the body such as the lungs, kidneys, larynx, meninges, and so forth. Eleven of the

17 patients had active pulmonary tuberculosis at the time of operation. Eight of the 17 obtained union and were free of all trouble with the knee. Two were subjected to amputation later. Of the 63 patients operated on since the original series of 211 cases was reported, 3 have died, from a year to two and a half years after the operation. Of the entire 274 patients comprising the two series, 9 per cent died. It has already been said that most of the deaths in the earlier series were the result of tuberculosis. The same applies to the second series as far as we could determine. In all, 248 patients were traced. Fusion resulted in 220 of these (88.7 per cent). Non-union developed in but one of the last 63 cases, whereas it resulted in 11 of the previous 211 cases. One negro, aged thirty-five years, with large, bony abscesses, still had draining sinuses three years after operation, but the knee was solid.

### ARTHRITIS

Arthroplasty is done to produce motion in an ankylosed joint. In the case of the average man who has a stiff knee that is in suitable position for use, it is rather debatable whether he should be subjected to the risk of having an unstable and painful knee following arthroplasty. Men, more often than women, have to work under conditions that are not conducive to comfortable walking. A woman who does housework, spending all her time on smooth floors, gets along comfortably with a knee that, although it may be somewhat unstable, still is capable of sufficient motion to enable her to sit comfortably and to go up and down stairs easily. It is my practice to advise any man who comes with a stiff knee not to undergo operation if the knee is in a good position for walking. Only under exceptional conditions do I advise arthroplasty in such a case.

Arthroplasty has gradually assumed a merited position in the treatment of ankylosis of the knee joint. It is not applicable to every case of ankylosis, but the patient who has a stiff, ankylosed knee which is causing considerable disability, annoyance and mental worry is certainly entitled to have the question of arthroplasty carefully considered. The selection of cases must be carefully made. The patient should not be too young or too old; preferably he should be between the ages of twenty and forty years. Many factors must be considered: the type of infection; the stage of the disease of the knee at the time of consultation; the type of ankylosis; the patient's social status and his occupation; the question as to how well he can get about with his ankylosis; the moral fiber of the patient, which is an indication of his ability to push through the painful aftercare and treatment, and lastly, the question of whether he will be satisfied with only partial function, which is really the best he can expect, or whether he will expect full, normal range of motion.

We have made a review of 78 patients, 21 males and 57 females, on whom eighty operations, arthroplasty of the knee joint, were performed. Six patients were not traced, but the results secured by 72 patients, on whom seventy-four operations were performed, are known. The questions that we tried to determine were as follows: (1) whether those with bony ankylosis or those with fibrous ankylosis secured the best results; (2) whether the ankylosis following gonorrhea gave any better or any poorer results than when the infection was from other causes; (3) whether patients with generalized infectious arthritis, that is with involvement of several joints, secured as satisfactory results as patients with monarticular involvement, and (4) whether patients whose stiffness of the knees followed trauma, such as intra-articular fracture, were as suitable subjects for arthroplasty as were those whose ankylosis was the result of infection.

Taking the group as a whole we found that 48 of the 74, or approximately 65 per cent, obtained satisfactory results: 27, excellent results, and 21, good results. Results were fair in 9 cases and poor in 17 cases. There seemed to be no particular

difference in end-results in the cases of bony ankylosis as compared with the cases of fibrous ankylosis. In both types of cases bone must be removed to permit of motion. In cases of ankylosis following gonorrheal infection, results were just as good as in cases following any other infection. The poorest results were obtained in cases of generalized infectious arthritis. One never knows when this disease is sufficiently quiescent, and many patients who underwent arthroplasty of the knee, before or later underwent other extensive procedures necessary to allow the knee to be straightened, such as osteotomy, arthroplasty on the hip or elbow, and so forth. Of those patients among whom involvement was of the knee only, 70 per cent obtained satisfactory results, as compared with less than 50 per cent of the general group. Patients who had ankylosis, either fibrous or bony, following intra-articular fractures of the knee joint did not obtain especially good results. Too often the callus reformed, and the patient was left with no particular improvement.

All pain, swelling, local warmth, and tenderness must have been absent for at least a year before operation is attempted.

Fig. 3. Postoperative arthroplasty splint and method of use.

*Types of Operation.* The principle behind all types of operation is the same; that is, excision of enough bone to permit of motion, remodelling of the ends of bone, and interposition of some substance to prevent ankylosis from recurring. Putti, endeavoring to reproduce the anatomic structure of the knee joint as closely as possible, shapes the condyles so that they will fit into the upper end of the tibia in as nearly as possible the normal manner. Campbell does not pay such strict attention to the anatomic structure of the resected joint, but makes one large condyle fit into the upper end of the tibia. Putti and Campbell both use fascia lata as an interposing membrane, whereas the late W. S. Baer used chromatized pig's bladder. Experience alone teaches how much bone to remove, but it is a general opinion that slight hyperextension at the completion of the operation should be possible when the ends of bone are finally reshaped.

The types of incision vary: some surgeons make a straight median incision; others a slightly curved incision, running to one side of the patella; still others, a transverse incision. Fascia lata may be obtained from the same leg or from the opposite leg. The period of postoperative fixation varies, but ordinarily movement is started within two weeks from the time of operation; various types of splints are used to allow this. The patient is encouraged to carry on the motion within two weeks by aid of an arthroplasty, hinged splint (Fig. 3). Physiotherapy, in which active and passive movements are employed, is of great aid. However, in the postoperative period it is common to find that at the end of about four weeks the patient is beginning to lose mobility, the joint becomes more tender, and both patient and surgeon are discouraged. It is at this period that manipulations under anesthesia are of value, and in addition, if necessary, adhesions are sectioned by a tenotomy knife. If the adhesions are very firm they should be severed, for too much manipulative force may produce a fracture or may injure the soft, new articulating surfaces of the bone ends. Sometimes, bony spurs form posteriorly, and they must be removed. Tightening of the quadriceps muscle may occur, so that lengthening, according to the method of Bennett, may be necessary. Postoperative care is difficult, taxing the ingenuity and resourcefulness of the surgeon. Intra-articular adhesions must be prevented; the capsule must be kept loose and the muscles active. The patient must coöperate, and must be willing to work hard to obtain motion, in spite of pain, or a good result will not be obtained.

Almost total synovectomy of the knee joint is possible, because the thinness of the covering over the joint makes the joint easily accessible. This measure is indicated in certain cases of arthritis in which there is little, if any, bony involvement, the thickening involving the synovia and capsule. Our experience with this operation has not been such as to make us overly enthusiastic. I think that some of our poor results can be explained by the fact that we operated on patients who were in the active stage of chronic infectious arthritis. Our best results have been in certain types of monarticular involvement.

In one case in which synovectomy was performed on both knees, tuberculosis was proved to be present in both, by microscopic examination and by inoculation of guinea pigs. An excellent result was obtained and now, two or three years after the operation, the patient is able to walk considerable distances with comparatively little discomfort. This same patient also had synovial involvement of the elbow joint, which proved to be tuberculous.

Synovectomy was performed sixty-four times on 58 patients. It is difficult definitely to tabulate the results in this series. There were 16 females and 42 males. The results were determined in 56 instances and were excellent in 13 and good in 13; that is, good results were obtained in 26 cases (46 per cent). Results were fair in 13 cases and poor in 17. The condition was limited to the knees in 24 cases and was generalized in 27. At operation in 24 cases it was noted that the cartilage was eroded.

Synovectomy was performed for synovial tuberculosis five times on 4 patients. In 2 cases it was found, at the time of operation, that the cartilage was eroded, and involvement of bone was suspected; in both resection was performed subsequently. The other 2 patients, one of whom had double involvement, are well and comfortable some years after synovectomy. This experience would indicate that in certain cases, in which the tuberculous involvement is purely synovial, synovectomy is well worth while. The difficulty is in determining the presence or absence of involvement of bone.

In performing synovectomy the joint is exposed by a long, anterior incision which runs along the inner border of the patella, so that the patella can be reflected outwards. The incision runs well up into

the quadriceps muscle and well down onto the insertion of the patellar tendon. The thickened synovia is then dissected out, and oftentimes, although not always, the internal and external semilunar cartilages are removed, depending on the degree of involvement. All the synovial membrane, except that in the posterior compartments, can be removed. The knee is kept in a cast that extends from the groin to the ankle, for approximately one week. At the end of this time motion is begun on a postoperative-bed-arthroplasty splint. It is preferable to start motion early. Sometimes, effusion of thin, blood-tinged, serous fluid occurs, and if this fluid is not absorbed within a short time, it should be aspirated. The patient should be encouraged to use the knee as soon as possible.

## DERANGEMENTS OF THE SEMILUNAR CARTILAGES

The most common cause of derangement of the knee joint is injury to the semilunar cartilages. The semilunar cartilages are partially fibrous, and they rip or tear longitudinally rather than being fractured transversely. In The Mayo Clinic we have tabulated the records of 309 patients who were operated on for derangement of the knee joint due to injury of the internal or external cartilages.

Injury to the internal cartilage is much more common than injury of the external cartilage. In our series the ratio was 10.4:1. The 309 patients were subjected to 315 operations. The results are known in 298 cases (96.44 per cent). The fact that the internal semilunar cartilage is so frequently injured can be explained on the basis that it has no lateral mobility, for it is firmly bound to the capsule and so to the internal lateral ligament. If it is caught between the internal condyle of the femur and the head of the tibia when the act of extension is under way, it cannot escape and is ripped, as a rule in its longitudinal axis. As this rip or tear occurs, the central margin is forced over into the internal condylar notch, remaining attached anteriorly and posteriorly, and making what was described many years ago by Rutherford Morison as a bucket-handle fracture. It is likely, I believe, that most of the tears and injuries of the internal cartilage are primarily of this type, and that further injury converts them into various other types (Fig. 4).

Injuries to the semilunar cartilages may be divided into four main types:

1. A tag-like flap, of varying size, may be split off from the anterior portion, and hang free, with base attached to the posterior mesial portion of the anterior third.

2. The same type of pedunculated flap may be seen in the middle third of the cartilage, sometimes doubled back on itself and pointing posteriorly. Such a flap may be worn into an ear-shaped tag, attached by a rather small, short pedicle. When caught, it causes sharp, severe pain, but is usually released readily if the patient gives a vigorous kick or two, and swelling or disability does not follow. I am confident that many times these ear-shaped tags are overlooked at operation because they are rather deeply situated, and not easily seen. In this event, the cause of the attacks is attributed to the more or less mythical fat-tags.

3. The bucket-handle or loop type of injury, which has been mentioned, causes the most constant symptoms, and generally is readily diagnosed.

4. A pedunculated flap, in the posterior third of the cartilage, often gives rise to bizarre symptoms. Through an anterior incision, it generally is impossible to see anything of a flap that is in this position, and it is not until the cartilage is removed, or a posterolateral incision is made to explore the posterior portion of the cartilage, that the lesion is discovered.

Injury to the semilunar cartilages is not so common in the United States as it is in England, because a far greater proportion of the British people than of our people indulge in athletic pursuits, and British coal miners work in low seams necessitating a crouched position with the knees flexed

and feet everted. Injury to the semilunar cartilage is always produced by indirect trauma, and usually while the patient is engaged in some active occupation or sport. However, I have seen several patients whose knees became locked for the first time while they were in bed. They had typical bucket-handle fractures, and the locking occurred when they merely turned over.

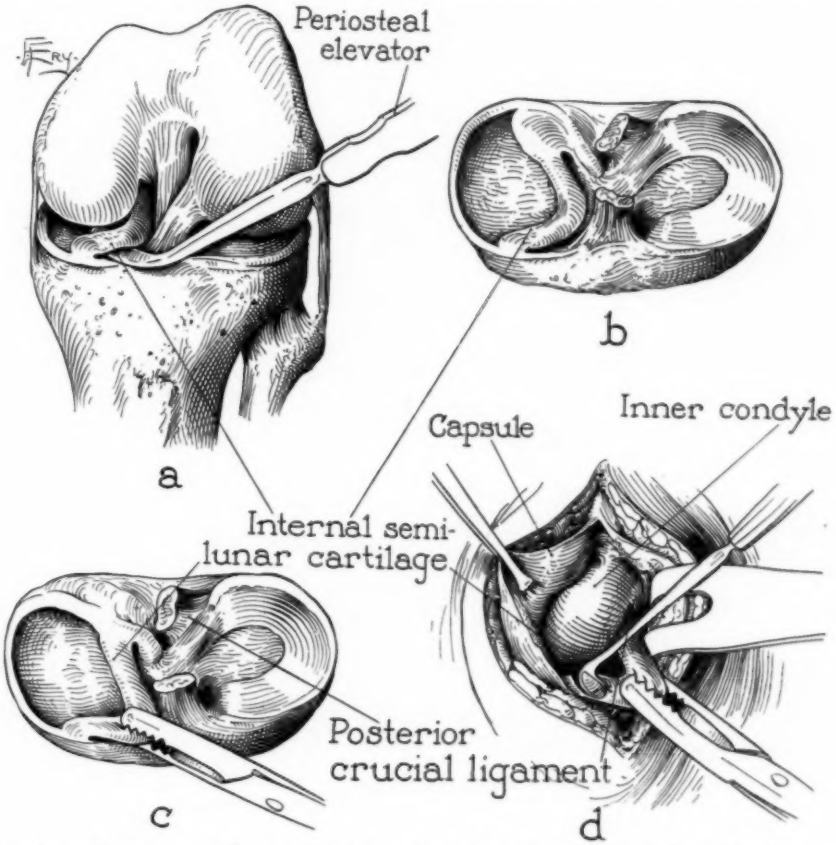


FIG. 4. Bucket-handle or loop type of fracture of internal semilunar cartilage; *a*, loop lifted up on elevator; *b*, loop displaced mesially; *c*, loop pulled forward; *d*, relation to internal condyle.

*Symptoms.* The symptoms, to the surgeon at least, are chiefly subjective, for he rarely sees the patient when the joint is locked. He must depend on the history, and therefore, in industrial cases one must be on guard. The patient's account of the happening at the time of the original injury is often indefinite, either because of the rapidity with which the injury occurred or because of lack of observation. The history commonly given is that the patient was injured during some more than usual activity. The happening was characterized by pain in the knee, coming on suddenly, accompanied by immediate inability to extend the knee (locking), and followed by swelling. Attacks of a similar nature occurred later, at irregular intervals, and were accompanied by more or less effusion in the joint. Between attacks the normal condition was completely restored. In our series of cases, in instances in which normal function was not restored between the attacks, it was found, in most instances, that there was a bucket-handle type of fracture, the loop failing to slip back from the intercondylar notch, thus preventing extension, although all other signs, such as pain, soreness and swelling, subsided, leaving the patient, however, with a feeling of insecurity in the knee. When he was told to stand erect, with both feet close together, and to straighten both knees, the affected knee could not be

completely straightened, and when it was pushed backward he complained of pain. In these typical cases the accident occurred with the knee partially flexed, the foot everted, and the strain clearly on the internal lateral ligament.

*Diagnosis.* In making the diagnosis, Kleinberg has suggested inflation with oxygen and roentgenologic examination. I have had no experience with this but it may be useful in certain cases.

The main points to be considered in the diagnosis have been mentioned. However, these points are: (1) injury to the knee, generally indirect, and sustained usually during some active pursuit, and (2) recurrent attacks with intervals of complete freedom both subjectively and objectively. The attacks are characterized by pain, disability, swelling, lack of complete extension, a feeling of something amiss in the joint, and usually some tenderness (if the injury is to the internal cartilage) over the anterior border of the internal lateral ligament at the joint line. In cases in which the external cartilage is the seat of the injury, the pain and tenderness are usually referred to the outer side.

The differential diagnosis is not always easy, but the condition must be distinguished from mild, chronic arthritis in which a swollen synovial membrane occasionally may become caught between the bones at the periphery. In arthritis, more than one joint often is involved. Osteocartilaginous bodies cause locking which is more transient than that of injury to the semilunar cartilages. Effusion rarely follows the locking seen in cases in which osteocartilaginous bodies are present, and finally roentgenograms disclose the offending bodies. Osteochondritis dissecans, especially in its early phases, may be confused with injury to the semilunar cartilages, but if the former condition is present, the roentgenogram usually discloses it. Recurring dislocations of the patella sometimes present difficulty in diagnosis but such dislocations usually affect women and the patient is usually able to recall that the patella became dislocated outwards.

*Statistical Study of Semilunar Derangements.* Of the 309 cases, in 282 involvement was of the internal semilunar cartilage; in 27, the external semilunar cartilage was involved. In 6 of the cases in which the internal semilunar cartilage was injured both knees were involved, and in one of these cases both internal semilunar cartilages were removed at the same time; the patient was a young woman. The typical history, that previously has been described, was obtained in 221 of the cases in which the internal semilunar cartilage was injured (76 per cent), whereas of the patients whose external cartilages were injured, 18 (66 per cent) gave typical histories. Flexion deformity caused by locking was present at the time of operation in 113 cases (39 per cent) of those in which the internal cartilage was injured; this sign was present in 6 cases (22 per cent) in which the injury was of the external cartilage. A clear-cut history of the accident having occurred while the knee was in flexion was given by 199 (69 per cent) of the patients whose internal semilunar cartilages were involved, and by 17 patients (63 per cent) whose injuries were of the external cartilages. Definite fracture of the cartilage was demonstrated at operation in 189 cases (65 per cent) in which the internal semilunar cartilage was injured, and in 14 cases (52 per cent) in which the external semilunar cartilage was injured. A bucket-handle type of fracture was present in 115 (40 per cent) of the cases in which the injury was of the internal semilunar cartilage and in 8 (29 per cent) of the cases in which the external cartilage was injured. Various other types of tears and fractures were encountered, but notation of the exact situation was not made in enough cases to permit me to present the data.

Of the patients, 252 were males and 57, females, a ratio of 4.4:1. The condition was more common among patients of the second and third decades of life than among those of other ages; 216 of the patients were between twenty and forty years of age. The average duration of symptoms before operation was 3.84 years.

*Comment and End-results.* Considering the patients whose injuries were of the

internal cartilages, together with those whose injuries were of the external cartilages, 229 (77 per cent) were relieved of all symptoms. The condition of 42 (13.59 per cent) was improved, although they were not relieved of all symptoms. Of 27, the condition was not improved. The results were somewhat better among patients whose internal semilunar cartilages were injured than among those whose injuries were of the external cartilages. When positive pathologic change was found, the percentage of cures was high, but when the statement was found in the surgical notes that the pathologic change was insufficient to account for the symptoms, the percentage of cures was decidedly lower.

What was considered to be definite pathologic change, either a fracture or a definitely loose semilunar cartilage, was found in 79 per cent of the cases, but even in the cases in which positive pathologic change was evident, satisfactory results were not always obtained. Of 203 cases in which fracture was definitely demonstrated at the time of operation and the cartilages were removed, in 186 (91.6 per cent) complete relief was produced; 17 patients (8.3 per cent) failed to obtain much relief and were recorded either as improved or not improved. This, I think, can be explained on the grounds that many times, in injury of the knee joint, the injured semilunar cartilage is only part of the trouble. Consequently, I have become increasingly careful, before operating on patients, to examine them very carefully for stability, both lateral and anteroposterior. If instability is found I explain to them that, although we can relieve them of the catching and locking, the probabilities are that a certain degree of instability will continue to be a source of annoyance. If pathologic change in a cartilage is not found when the joint is opened, prognosis should be guarded, for in a large proportion of cases benefit fails to follow removal of a cartilage that appears normal at exploration.

If the crucial ligaments are injured to such an extent that a really unstable knee is present, some form of reconstruction of the crucial ligaments could be undertaken. Krida recently has reported some interesting and instructive cases. My experience with this operation is limited to such a few cases that I cannot speak with any authority on the procedure.

### RECURRING DISLOCATIONS OF THE PATELLA

Recurring dislocations of the patella are much less common than semilunar injuries, but are to be reckoned with in making a diagnosis of derangement of the knee joint. The patient is usually a young woman who gives a history of sudden, excruciating pain in the knee, with immediate disability. The patient may be so overcome by the severe pain that she does not know just what happened or what the appearance of the knee was at the time of the accident. In the comparatively few cases that I have had the opportunity of seeing when the dislocation occurred, the diagnosis was self-evident. The patella was lying well to the outer side of the external condyle, while the internal condyle was abnormally prominent, and the knee was flexed to about a right angle. The dislocations in the series of patients on which these remarks are based were all to the outer side. Occasionally the dislocation is to the inner side, but I have never seen it. A familial history may be obtained.

The dislocation is readily reduced by straightening the knee and pressing the patella back toward its normal position; it goes into place with a crunching snap. Considerable effusion into the joint and ecchymosis in the skin commonly follow. The frequency with which the dislocations occur varies greatly; the patient usually seeks relief as they become more common.

Thirty-five patients, of whom 30 were females and 5 males, have been operated on at The Mayo Clinic. Thirty-nine operations were performed on these 35 patients; both knees were operated on in 4 cases. The results were determined in 35 cases, and it was found that no further dislocations occurred in 33 (94 per cent).

*Operation.* Various types of operations have been devised. Goldthwait, many years ago, described a method of plastic

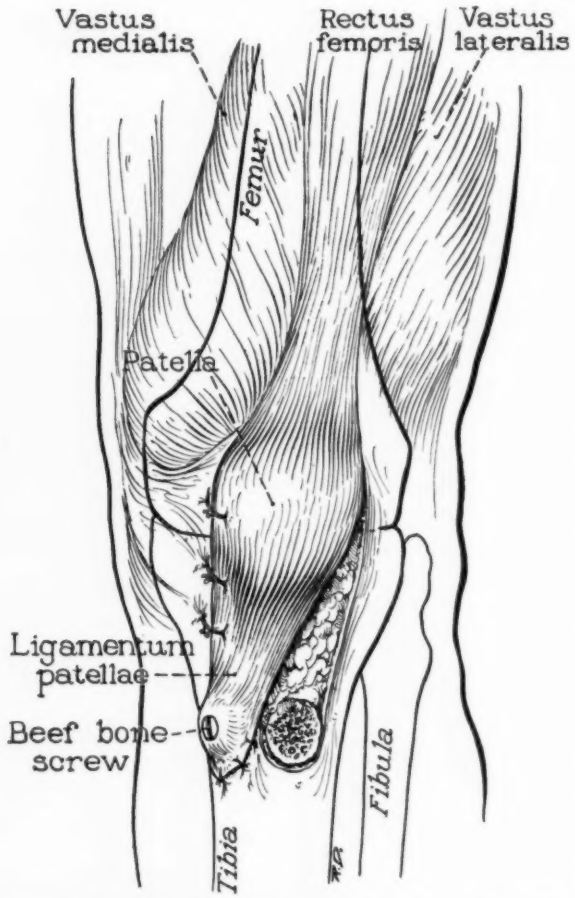


Fig. 5. Operation for recurring dislocations of patella. Transference inward of insertion of quadriceps.

operation on the patellar tendon. Albee has advocated the use of a bone graft, forcing upward, and raising to a higher level, the external condyle. Gallie has used fascia lata as a check ligament. All these operations have merit, but I can speak with any authority only of the operations we have used.

Our operation consists of transference of the insertion of the patellar tendon well to the inner side of the tibia and at the same or a slightly lower level. A flake of bone of good size is lifted up with the tendinous insertion; it is placed on a denuded area on the inner side of the tibia, and is held there by the aid of a beef-bone screw. This is further reinforced with sutures of chromic catgut, lengthening the capsule on the outer side and overlapping it on the inner side (Fig. 5). I believe, if this technique is accurately carried out, and if protection is afforded long enough after operation, that cure is practically assured. We have used fascia lata in 3 cases, with failure in one, and it was after this failure that I adhered closely to the plan of shifting the position of the tendon.

Following the operation, the knee is put at rest in a plaster-of-Paris cast that extends from the groin to the ankle. The knee is held in position for at least three weeks before motion is started. Then motion is begun gradually; flexion to a right angle is not permitted for at least three months. Shifting of the tendon alters the mechanics considerably, and some patients complain a good deal of stiffness and of pain. However, this gradually wears away, although six months to a year may be required for it to disappear. The stiffness and pain do not constitute serious objections to the operation. In my experience, if the insertion of the patellar tendon has been moved far enough inward and held there until it has become firmly attached, dislocation of the patella has been impossible. The few failures encountered were due to permitting too early motion, causing shifting of the point of insertion.

## SUMMARY

I have presented some of the important surgical conditions of the knee joint.

The percentage of cures and satisfactory results following arthrodesis for tuberculosis is high.

Arthroplasty for ankylosis is now well standardized and sufficiently good results can be obtained to warrant its use in properly selected cases.

Synovectomy, in our experience, has not been as satisfactory as we would wish. We are employing it with more caution and less often than formerly.

Removal of fractured, torn, loose or injured semilunar cartilages gives a high percentage of good results.

Operations for dislocations of the patella may be undertaken with great confidence.

# AIR-CUSHION REDUCTION OF INCOMPLETE VERTEBRAL FRACTURE DISLOCATIONS

## ASSOCIATED WITH SPINAL CORD INJURIES*

BYRON STOOKEY, M.D.

NEW YORK CITY

REDUCTION of incomplete fracture dislocations of the vertebrae associated with spinal cord compression is rendered difficult because of the injury to the spinal cord and the danger of pressure sores and trophic disturbances. Acute injuries of the spinal cord are frequently followed by such marked trophic disturbances that the application of plaster or other fixed forms of reduction are undesirable especially in the first few weeks following the injury and often for longer periods.

The method presented can be used immediately after the injury, can be maintained as long as may be desired, and is available in any hospital having an air mattress. Reduction of the dislocation is accomplished without manipulation and usually no special skill is required.

When applied to incomplete fracture dislocations of the cervical region the principle involved is gradual and continuous overstretching of the neck musculature with the head dependent and the neck in hyperextension. Within a few hours the muscles are completely relaxed and reduction takes place.

The occiput is placed in a dependent position by bending the head end of an air mattress acutely over a blanket roll (see Fig. 1). This is very simply accomplished by placing an 8 inch wide strip of adhesive to the air mattress at the level of the blanket roll, pulling down on the adhesive as tightly as possible and fastening it to the bed.

The same principle of acute angulation may be applied to any part of the spine to obtain hyperextension by altering the position of the adhesive and the blanket roll beneath the air mattress. The method is thus applicable to compression fractures of the spine whenever air-cushion hyperextension is desired. The use of an air-cushion hyperextension in most cases is preferable to the canvas-covered Bradford frame or its modifications. The degree of hyperextension may be varied by the size

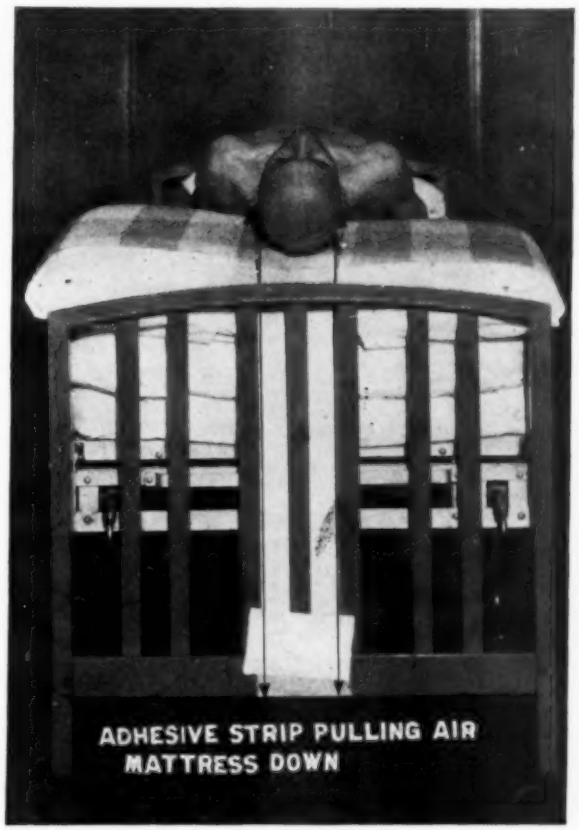


FIG. 1.

* Read before the Section of Orthopedic Surgery, New York Academy of Medicine.

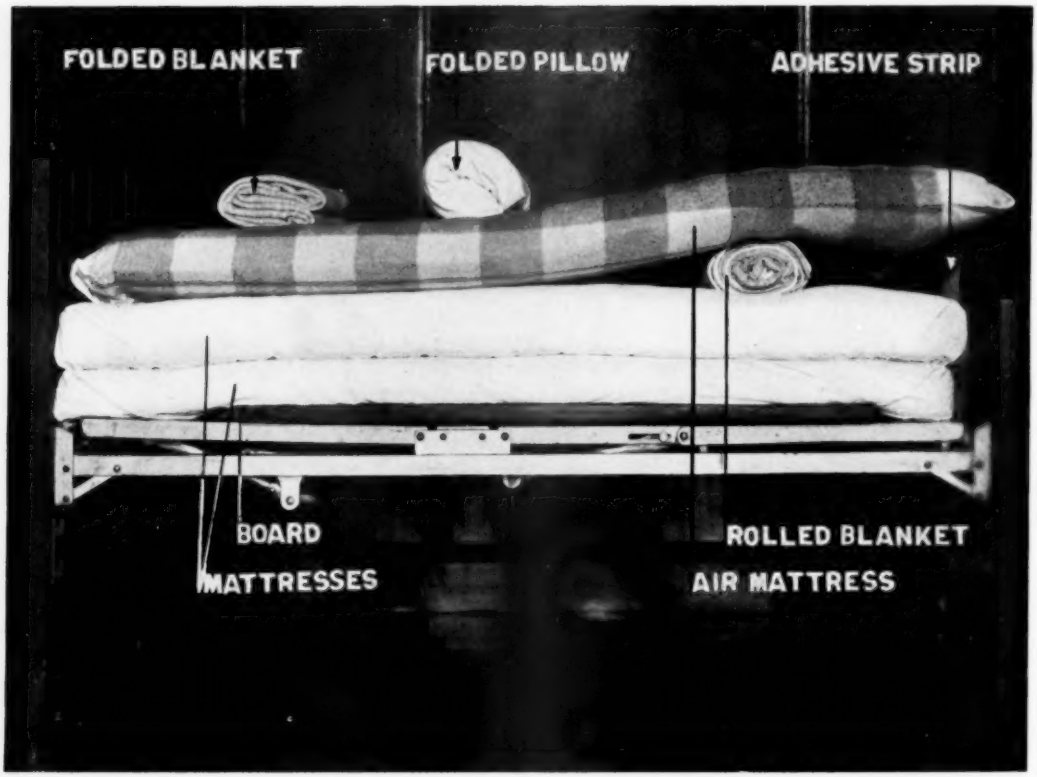
FOLDED BLANKET
FOLDED PILLOW
ADHESIVE STRIP
BOARD
MATTRESSES
ROLLED BLANKET
AIR MATTRESS

FIG. 2.

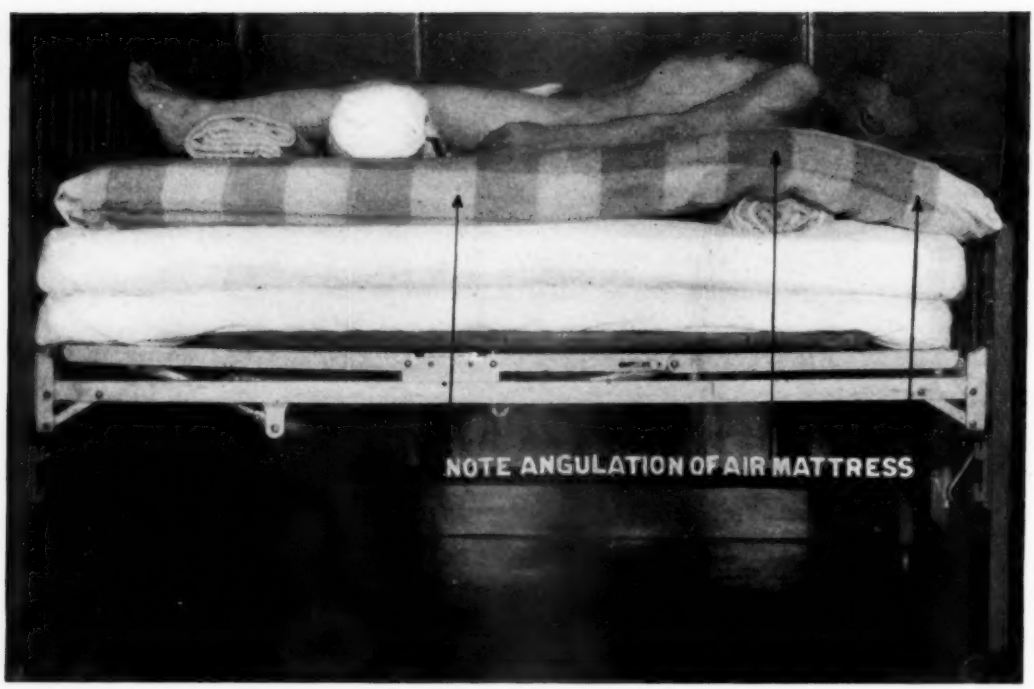
NOTE ANGULATION OF AIR MATTRESS

FIG. 3.

of the blanket roll and the level of hyperextension by the position of the blanket roll.

With slight modifications the principle of this method may be used for transporting patients with acute spinal cord injuries by substituting a stretcher for the bed and using an air mattress, either narrow or wide, and a blanket roll in the same manner. If an acutely injured patient is placed immediately upon an air mattress and stretcher, further injury of the spinal cord by handling in moving is avoided and pressure on the cord is minimized. The patient is in hyperextension and in a position to favor reduction even while being transported and prepared for *x*-ray and more permanent care. Inept handling of fracture dislocations in the process of transportation may further displace the vertebral fragments and injure the spinal cord still more.

The technique used is as follows:

(1) A fracture board is placed on the springs in the usual manner. The foot end of the bed is placed on low blocks to elevate slightly this end of the bed in order to raise the relative position of the patient's head to his trunk.

(2) In order to have the head easily accessible the foot end of the bed is made the head of the bed and two ordinary mattresses are placed over the fracture board to raise the level of the patient's head above, or at least level with the top of the foot piece.

(3) A blanket is then rolled and placed upon the ordinary mattresses at the level of the shoulders for fracture dislocations of the cervical vertebrae or at whatever level may be indicated for fractures of other regions of the spine.

(4) A thick air mattress, preferably 8 inches thick (a thinner air mattress is unsatisfactory), is then placed upon the bed over the blanket roll and an 8 inch wide strip of adhesive, if the fracture is in the cervical region, or a 12 inch to 14 inch wide strip, if the fracture is in the thoracic or the lumbar region, is applied to the mattress beginning at the line of the blanket roll. (Fig. 2.)

(5) The mattress is covered with a soft woolen blanket or a sheet, if preferred, and the patient is then placed on the bed. A soft woolen blanket absorbs moisture and in my experience is more comfortable for the patient than a sheet.

(6) The adhesive is then drawn as tightly as possible using as much force as necessary to obtain the proper degree of angulation of the air mattress. The adhesive is then fastened to the bottom of the foot piece of the bed either directly or to a movable bar attached to the foot end using a ratchet to tighten as needed. The air mattress must not leak, must be kept pumped up, and the adhesive must be tight at all times. (Fig. 3.)

(7) A pillow is then rolled and placed beneath the patient's knees so as slightly to flex the lower extremities. A small folded blanket is placed beneath the calf muscles reaching to within 4 inches of the insertion of the tendon of Achilles. The heels are thus kept off the bed by resting the calves on a wide surface and pressure sores of the heels are thus avoided. In my experience so called "small doughnuts" are most unsatisfactory in keeping pressure off the heels.

Any abnormal position of this sort is naturally uncomfortable and in my experience I have found it advisable to relieve the patient's discomfort during the first few days by medication, such as codein and luminal. As the patient becomes accustomed to his position, the drugs may be discontinued.

If each of the details is carefully observed I believe that this method will be found satisfactory for the reduction of incomplete vertebral fracture dislocations, especially in the cervical region, and for the reduction of compression fractures of the whole spine. Its simplicity and availability, wherever an air mattress is to be had, are additional factors to commend it both as either temporary or more prolonged means of reduction, or for transportation of acute injuries of the spinal cord associated with fracture dislocations of the vertebrae.

# EVIPAL SODIUM: A SHORT INTRAVENOUS ANESTHESIA

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EVIPAL anesthesia, extensively used in foreign countries, particularly Germany and Great Britain, is still little known in America. To the present time only one clinical report has appeared on the use of the drug in this country.[1] In contrast, an extensive foreign literature offers reports on more than 50,000 administrations of this form of anesthesia.*

Based on the reassuring nature of the literature we have conducted a clinical study of the drug with particular care to test its applicability in a wide variety of surgical conditions. The material for the paper consists of the records of 280 evipal anesthesias at Bellevue Hospital, the New York City Cancer Institute and in private practice.

## THE DRUG

Evipal is, chemically, N-methyl cyclohexenyl-methyl-malonyl-urea (Cyclural). It was isolated in 1932 by Kropp and Taub in the course of experiments on barbituric acid derivatives and its pharmacologic actions were soon established by Weese.[2] For anesthetic purposes the sodium salt of the drug is employed. It is a water soluble powder, supplied in 1 gram sterile ampules which are dissolved at the time of use to form a 10 per cent solution for intravenous injection. The striking features about evipal are the ease of administration, the rapidity of onset of surgical anesthesia, the smoothness of induction, the wide margin of safety, and the prompt recovery without disagreeable postanesthetic by-effects.

The clinical action of the drug is best described by a typical example of its use: As the injection begins the patient becomes drowsy, his conversation lags and within the first minute he falls quietly into a deep sleep. There is no asphyxia, discomfort, excitement or struggle. The respirations become deeper and often slower. The jaw drops and muscular relaxation sets in early. Operation may begin at once. The color remains unaltered. The pulse is full and regular, and sometimes slightly increased in rate. The blood pressure falls from 5 to 20 mm. mercury with the onset of sleep, then rapidly returns to normal. The time of awakening depends upon the dose administered and is usually within from ten to twenty minutes. There is no postoperative excitement; the patient remains drowsy and if undisturbed, falls asleep for an added period. Nausea or vomiting do not occur. The subject has no recollection of anything which has transpired after the initial needle-prick. For the surgical procedure of short duration it would be hard to imagine a smoother or more satisfactory form of general anesthesia.

Detoxification is so rapid that despite its non-volatile nature evipal sodium approaches closely to the controllable type of inhalation anesthetic. Half the injected amount is eliminated within the first fifteen minutes. The detoxification occurs in the liver, where the drug is almost completely metabolized by chemical disintegration; only faint traces of the unchanged drug are found in the urine. Evipal has a high therapeutic quotient in experimental animals. The lethal dose has been demonstrated by numerous inde-

* In all countries except the United States and Canada this product is sold under the trade name "Evipan."

pendent investigators to be 3.3 to 4 times the full anesthetic dose.[3]

The accompanying graph, after Anschütz,[4] illustrates the rate of induction, depth and duration of evipal anesthesia as contrasted with ether and avertin. The plotted curves emphasize the unusual speed of onset, the profundity of anesthetic action and the rapidity of recovery in evipal narcosis. (See Fig. 1.)

The drug is not entirely free from undesirable effects. Deliberate lethal doses produce death by respiratory failure. At times under full therapeutic doses some respiratory embarrassment may occur either by central action or because of a falling backward of the tongue. Transient twitchings have been noted during induction. Excitement occurs in about 1 per cent of cases. In rare instances, particularly with very slow administration, the detoxification rate is sufficiently rapid to prevent the attainment of full anesthesia. The outstanding characteristic of the action of this drug in contrast to that of most other anesthetic agents is the shortness of duration of anesthesia, which usually lasts only from five to twenty minutes, varying with the dose, type of patient and technique of administration. This factor necessitates, for the successful use of the drug, deliberate limitation to such procedures as may be completed within the time limits of its pharmacologic action.

### Technique of Administration; Dosage

The drug is dissolved within its ampule by adding 10 c.c. of sterile triple distilled water, yielding a 10 per cent solution. The solution should be clear; any undissolved particles indicate decomposition of the product, which should be discarded.

To take full advantage of the short evipal anesthesia and to reduce the required dose the surgeon and his instruments must be ready and the operative area prepared and draped before the administration begins. A tourniquet is applied to the arm and, after due antiseptic precautions, injection is made into one of the veins of the antecubital fossa. When the needle is in the vein, as proved by the free aspiration of blood, the tourniquet is

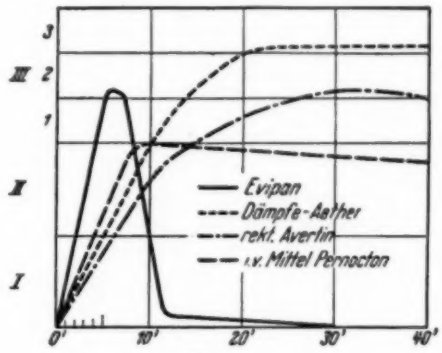


Fig. 1.

released and injection begun. The use of a small hypodermic needle to enforce slow inflow of the drug is recommended. Speed of injection is controlled by timing with the second hand of a watch. When a fractional technique is employed it is well to have close at hand a second hypodermic needle in case blood should clot within the lumen of the first.

When the total dose to be administered is small (3.5 to 5 c.c.) this is injected in one minute and the needle withdrawn. For larger doses it is advisable to give half of the intended maximum dose within the first minute, leaving the needle in the vein and giving additional fractional doses of 1 c.c. as required to maintain adequate anesthesia or until the predetermined maximum dose has been given.

The dosage scheme suggested by the manufacturers (from 7 c.c. of the 10 per cent solution for a 110 pound patient to 10 c.c. for one of 165 pounds or over) may be taken as the reasonable average maximum clinical dose. Rigid mathematical doses, however, are no more proper for evipal than for ether; the total dose must be decreased for old age, debility, cachexia, sepsis, toxicity and the presence of marked obesity or edema. From 3.5 to 5 c.c. have proved adequate for minor procedures in the average adult requiring from five to ten minutes of narcosis. For longer operations, from 6 to 10 c.c. will usually give anesthesia lasting fifteen to thirty minutes

or over, full duration depending on premedication, later discussed.

### SAFETY FACTOR

Evipal sodium has passed the experimental stage. The Medical Research Council of the Royal Society of Medicine, of London,[5] in reporting on the clinical value of evipan, quote reports of "twenty-five thousand cases . . . with only one death attributed to evipan." Numerous large case-series demonstrate the relative safety of this anesthetic. Jarman and Abel[6] report 1000 cases without a death, Jarman[7] gave an additional 1400 anesthesias without a death; Holterman[8] reports 2000 cases with one death; de la Camp Bürkle[9] 1000 administrations without a death; Friedeman 600 cases without a death; Samuel 500 cases without a death; Westerborn 500 cases without a death; Baetzner 400 cases without a death; Anschütz 400 cases without a death.

Anschütz, in reporting his 400 personal cases without a fatality,[4] made a survey of all deaths in patients who had received the drug to that date (April 18, 1933). In twenty-five series totaling 6460 evipan anesthesias he found 4 deaths following the use of the drug. He adds 4 other isolated fatalities following an unknown total number of evipan anesthesias. Both Anschütz and subsequent writers who have studied these same cases accept only one as due to the drug (Stimpfl,[10] Med. Res. Council[5]). The remaining either had received the original form of the drug in solution in methylene glycol, now discarded; had definite overdoses; or presented now recognized contraindications to the use of the drug. The favorable report of the British Medical Research Council is a reliable guide to the great relative safety of evipal.

Despite the low mortality associated with evipal, an extensive review of the clinical and pharmacological literature with consideration of the reported anesthetic complications led us to set the following limits for this series: No evipal was given patients with extensive liver damage, with depression of the respiratory center, or with severe infections about the upper air passages. Extreme caution is exercised in patients with severe sepsis. Ten c.c. is our maximum single dose; 6 c.c. is not exceeded in debility, emaciation, circulatory insufficiency and severe infection. For children[11] our doses follow Young's rule. Evipal undoubtedly has uses well beyond these arbitrary limits, but it was on the basis of these limits that the present study has been made.

The cases on which this series is based are summarized in the appended self-explanatory chart. Although numerically this series is not large in comparison with certain foreign reports, the material presents such a cross section of surgical procedures and the results are so uniform and satisfactory that we feel the study has answered many of the questions arising at the outset of the investigation and may prove of value to others who have not made use of the drug or who have not reviewed the literature of the subject.

Study Chart of 280 Evipal Anesthesias

| | | |
|---|---|---|
| Minor Surgery | | 103 |
| Abscesses | | 16 |
| Carbuncles | | 6 |
| Felons and paronychia | | 9 |
| Removal of nail | | 3 |
| Debridement | | 4 |
| Painful dressings | | 14 |
| Dislocations | | 2 |
| Fractures | | 14 |
| Colles' | 6 | |
| Clavicle | 2 | |
| Pott's | 4 | |
| Elbow | 2 | |
| Tendon repair | | 4 |
| Extraction of foreign body | | 5 |
| Excisions | | 9 |
| Sebaceous cyst | 5 | |
| Lipoma | 4 | |
| Ingrown toenail | | 3 |
| Hand infections | | 8 |
| Palmar space | 6 | |
| Tenosynovitis | 2 | |
| Amputations | | 6 |
| (Of these cases 24 were in children) | | |
| Surgery in Cancer | | 67 |
| Endoscopies | | 5 |
| Radium insertions (seeds, needles) | | 24 |
| Excisions and biopsies | | 29 |
| Uterine tandems | | 9 |

| | | |
|---|---|---|
| Proctology | | 10 |
| Hemorrhoidectomy | | 4 |
| Fissure | | 3 |
| Rectal dilatation | | 3 |
| Gynecology | | 15 |
| Dilatation and curettage | | 11 |
| Excision of Bartholin cyst | | 4 |
| General Surgery* | | 40 |
| Appendectomy | | 2 |
| Herniorrhaphy | | 4 |
| Exploratory laparotomy | | 6 |
| Colostomy | | 7 |
| Gastrostomy | | 2 |
| Amputations | | 3 |
| Thoracotomy | | 1 |
| Ludwig's angina | | 1 |
| Simple mastectomy | | 13 |
| Abdomino-perineal resection | | 1 |
| G-U Surgery | | 13 |
| Cystoscopies | | 8 |
| Children | 6 | |
| Adults | 2 | |
| Meatotomies | | 2 |
| Circumcisions | | 3 |
| Orthopedics | | 3 |
| Arthrotomies | | 2 |
| Sequestrectomy | | 1 |
| Otolaryngology | | 4 |
| Drainage of antrum | | 1 |
| Tonsillectomy | | 1 |
| Myringotomy | | 2 |
| Surgery in the Diabetic | | 12 |
| Surgery in Tuberculosis | | 8 |
| Obstetrics | | 4 |
| Second stage labor | | 2 |
| Episiotomy | | 1 |
| Perineorrhaphy | | 1 |
| Dentistry | | 14 |
| Extractions | | 9 |
| Alveolectomy | | 5 |

* In association with regional or inhalation anesthesia, when required.

## DISCUSSION

Our experiences and impressions regarding evipal are best presented in the form of a few general observations followed by a more minute discussion of certain special fields of utility.

Perhaps the outstanding feature about the drug is its wide applicability. Our youngest patient was two years old, our oldest eighty-eight; the average age was forty-two. The patients ranged from vigorous healthy young individuals to the extremes of emaciation and cancerous cachexia. The drug was given in the presence of active tuberculosis, diabetes, nephritis and acute upper respiratory infection. Except for our predetermined limits (liver damage, respiratory difficulties and severe sepsis) no case needing a short surgical procedure was denied this anesthetic; excluding only these contraindications, this was a consecutive series given without regard to age, disease, or general condition of the patient.

In no single case did symptoms or signs arise that indicated imminent danger or caused alarm over the safety of the patient. In no instance did nausea or vomiting occur either during induction or after recovery. Postanesthetic headache and disorientation were not noted. Several patients were given evipal immediately after meals, and, in every case where the surgical condition did not contraindicate, full meals were allowed immediately after the anesthesia. Patients were allowed up and about, when their condition permitted, as soon as they completely recovered from the narcosis. Patients have repeatedly expressed their willingness to take evipal a second time for any needed operation, and those who have had experience with other forms of anesthesia have quite uniformly expressed a choice in favor of this drug.

Our experience with serious complications has been small because of the limitations we set ourselves as to dosage and absolute contraindications. About 1 per cent of cases showed excitement, twitchings and respiratory difficulty, in no instance severe. Isolated cases presented reflex motor responses despite complete analgesia. These movements are never remembered by the patient, but are objectionable to the surgeon because of the possibility of soiling the field. These patients should have their hands fixed as for any other general anesthesia. Slow administration, and commencing the incision before analgesia is complete seem definitely to intensify these phenomena. Should these responses occur when incision

is made, it is well to delay further operation for a half to one minute to allow full analgesia. One objection to evipal is the shortness of anesthesia, which necessitates careful case selection. There must be no hesitancy to supplement with other anesthetics when the operation extends beyond the anticipated period. In 12 cases in this series we resorted to gas-oxygen to complete the operation. One case of local subcutaneous inflammation with a slough occurred after accidental perivenous injection of 6 c.c. of solution. This was the only case in which difficulty was encountered in entering the vein. Thromboses were not noted.

One death occurred in this series, almost certainly not related to the evipal used:

> A man, twenty-five, with Ludwig's angina, temperature reaching 105°F., and pulse 140, was given 8 c.c. of evipal in fractional doses. There were no immediate complications. Death occurred ten hours later and was due to the infection, with no symptoms or signs attributable to the anesthesia.

This case occurred early in our series. Death took place many hours after the administration of evipal, the patient showed normal recovery from the anesthesia, he was well in the interim, and the disease is one with a recognized high mortality. Nevertheless, in the latter part of our series both severe sepsis and partial upper respiratory obstruction were conditions in which evipal was not further employed.

While it is our purpose to explore the actions of evipal rather than to make comparisons with other drugs, certain important differences are worth recording.

For a short surgical procedure in adult or child, the delay in induction when using ether, the slow recovery, the bronchial irritation, the postoperative vomiting; all seem unnecessary factors in the light of this new anesthetic which obviates each of these objectionable features. Evipal has a rapidity of induction and elimination of the order of gas-oxygen anesthesia but is free from the asphyxial tendencies of nitrous oxide. Several deaths have been reported from the administration of gas-oxygen in colored patients, in whom pigmentation made it impossible to recognize the color changes of cyanosis. This criterion is not needed with evipal.

The ease of administration, through a single needle puncture and the lack of necessity for any exact neuroanatomical knowledge are in sharp contrast with the technical difficulties, multiple needle punctures, mental upset and occasional failure that characterize nerve block. For apprehensive patients and children too young to cooperate, evipal anesthesia has marked advantages over regional methods. The lack of need for special apparatus, special anesthetist and highly specialized training is an extremely important consideration in favor of this short intravenous general anesthesia. A brief statement must be made on premedication and the use of evipal in conjunction with other forms of anesthesia.

The preliminary use of morphine definitely deepens and prolongs the action of this drug, and correspondingly increases any elements of danger which may exist. We feel that there should be no premedication for the minor surgical procedure of known short time requirement, and when premedication is deliberately used to extend the length and depth of anesthesia, the dose should be small (morphine sulphate gr. $\frac{1}{6}$) and the evipal administered in smaller or more carefully fractionated doses. It is well to insist that carbon dioxide-oxygen be available to stimulate respiratory activity should difficulty ensue on the conjoined use of these two respiratory depressants.

Typical of the use of evipal as induction anesthesia is the following: An exploration for carcinoma of the stomach is contemplated, but it is unknown whether resection, gastro-enterostomy or no procedure beyond the exploration will be chosen. In such case, evipal is given, the peritoneal

cavity opened, exploration conducted and the abdomen closed if the case is inoperable. If operation is determined upon, the abdominal wall and lesser omentum may be infiltrated with novocaine before the patient arouses from his evipal narcosis, or the anesthetist may turn to the use of ether or spinal for the completion of the operation. As an example of the use of evipal as a supplementary anesthesia may be mentioned its use at the end of a spinal anesthesia, when the effect of the subdural block has begun to wear off. It has been thus employed for the perineal phase of the abdominal-perineal operation for carcinoma of the rectum.

Space limitations prohibit a detailed discussion of all the fields in which evipal anesthesia has special utility. These will undoubtedly be stressed in separate articles by many authors as experience with this drug accumulates. We have tried to make the appended chart express for itself our experience in particular fields and we urge that the chart be studied from that viewpoint. For example in the treatment of malignant disease the drug has been used for excision of carcinomata of the lip, tongue, cheek, skin and cervix; for insertion of radium in the form of needles, colpostats, seeds and tubes; for diagnostic dilatation and curettage; and for biopsy excisions in all regions of the body. This relatively high percentage of neoplastic disease does not signify any particular applicability of the drug to cancer work, but is explained by the fact that so large a proportion of the anesthesias were given at the New York City Cancer Institute. In this consecutive series of cases our experience with evipal in fractures, minor surgery, and the other fields enumerated has been equally satisfactory.

## CONCLUSIONS

1. Evipal is a safe convenient general anesthetic which may be confidently employed, with but few specific contraindications, as a routine anesthesia for surgical procedures of short duration.

2. This intravenous anesthetic produces a remarkably rapid induction and is followed by a quick recovery, free from disagreeable symptoms and sequelae.

3. Evipal also has a field of usefulness for the surgical case of longer duration employed either in combination with other anesthetic agents or with premedication which prolongs its action; it may be used as an induction anesthetic, to be followed by inhalation narcosis, or may be given as a supplementary anesthetic in operations begun under spinal or regional methods.

4. The drug should not be employed in the presence of extensive liver damage or in the face of mechanical interference with the air passages and it should be used with caution in severe sepsis or with marked depression of the respiratory center.

5. Evipal has passed the experimental stage; its wide applicability, ease of administration, safety, and freedom from complications mark this drug as a permanent addition to our anesthetic armamentarium. Within its special sphere, evipal has distinct advantages over other forms of anesthesia now employed.

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CLINICAL RESULTS FROM THE USE OF A

# NEW AND SUPERIOR ANTISEPTIC SOLUTION

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ONE of the factors of paramount importance in the production of perfect surgical end-results is the antiseptic used. Yet how few surgeons really explore this field below or beyond the representations of enthusiastic salesmen or the attractive presentations of the manufacturer.

In the February, 1934 issue of THE AMERICAN JOURNAL OF SURGERY appeared a nicely worked out study of the comparative effectiveness of some thirty-two commonly used antiseptics.[1]

In the article referred to an isotonic solution of iodine was given the very highest rating and this led to a desire on my part to know more of the solution so rated.

After corresponding with the men who had developed this solution at the Mellon Institute in Pittsburgh I had a local pharmacist make up a quantity.

I then had it used liberally in the general hospital routine and in our out-patient clinic. Our surgical supervisor made personal observations and records of each case and this paper is presented to briefly set forth our findings during the past six months in the use of what seems to us an outstanding contribution to antiseptic solutions for general use in hospital, clinic and home.

What should be the essential properties of an ideal antiseptic solution for general hospital use?

1. *Effectiveness.* It must do the work desired. Whether used in the preoperative preparation of the abdomen or in an attempt to sterilize the cuts and abrasions of some victim of an auto accident, it must have the power to kill bacteria and do it promptly.

True, an antiseptic may be very effective in killing bacteria and yet be so irritating or destructive to the tissues as to make its use impractical, but the antiseptic solution that we will describe is rapidly effective yet possesses none of these undesirable qualities.

It has a phenol coefficient about 15 per cent greater than an alcoholic iodine solution of like strength.[2] When used for preoperative preparation of the abdomen the incision may be made in from fifteen to thirty seconds after the surface is painted. The surface is then clinically sterile. We have seen no stitch abscesses or other evidence of faulty skin sterilization.

The aqueous solution of iodine may be wiped from the skin surface in thirty seconds after it is painted on and a uniform penetration greater than that of any alcoholic solution of iodine can be demonstrated.

With this aqueous solution, uniform and quite exact dosage is possible while with the alcoholic solution that is allowed to stand in puddles and dry by evaporation the dosage is excessive at some points and insufficient at others.

Karns, Cretcher and Beal[2] claim that "excessive irritation causing destruction of tissue is usually due to a lack of adjustment of the dose between the amount of the active agent required to give adequate antisepsis and that causing tissue destruction."

This particular aqueous solution is superior to alcoholic solution of iodine in wetting power.[3] It penetrates the skin

deeper and more rapidly. In operations where the skin surface about the incision is constantly bathed in pus or abdominal secretions this deep penetration maintains the asepsis of the outer layers of the skin longer than alcoholic solutions do.

2. *Versatility*. An antiseptic solution to be universally applicable to the various needs of hospital service must possess some outstanding qualifications besides effectiveness. This solution is again our answer.

It may be used for preoperative skin preparation without as much danger of irritation or blistering as when alcoholic solutions of iodine are used. It may be used on mucous surfaces, as the vagina, rectum, mouth, nostrils, etc. In proper dilution it is a very excellent mouth wash and gargle and in this same dilution is a very satisfactory wet dressing. It may be used as a vaginal douche or for sinus irrigation.

When used in full strength on fresh wounds and surfaces denuded of epithelium very little, if any, smarting or burning is complained of and a mild degree of coagulation is noted which aids in the stopping of oozing. The freedom from smarting makes it a favorite with children who are so often dressed with less effective or even worthless agents because they do not smart or burn.

We have also found this new solution very superior where iodine absorption is desired as in some glandular conditions and respiratory affections.

We have painted the chests of children front and back, night and morning on several successive days and have not as yet noted any blistering.

3. *Economy*. Even in the best of times due economy is practiced in all well-regulated hospitals. An antiseptic solution for universal use must be inexpensive enough to permit of its use in adequate amounts. The cost of the aqueous iodine solution which we have used compares favorably with that of tincture of iodine and is materially less than that of the new proprietary substitutes.

Its stains on linens, wood work, floors, etc. are easily removed and do not damage the materials. It is promptly effective so that a small amount goes a long way and we find it the most economical antiseptic solution that we have used.

4. *Stability*. Alcoholic solutions change in strength due to evaporation of the solvent. Chlorine solutions are very unstable and must be freshly prepared. Some popular antiseptic solutions are changed by exposure to light. The new solution of iodine, however, is very stable and this adds to its economy.

## SUMMARY

It seems to us that an antiseptic solution possessing these four clinical qualities: effectiveness, versatility, economy and stability, should have wide appeal. No attempt has been made in this paper to consider the scientific basis upon which the new iodine solution rests nor the careful experimental work which led up to its perfection; this was set forth in a paper by George M. Karns[3] and in the paper by George M. Karns, Leonard H. Gretcher and George D. Beal.[2] It is our desire simply to call to the attention of surgeons the excellent results obtained by these workers at Mellon Institute and to endeavor to inspire an interest in the widespread clinical proving of what seems to us to be a very superior antiseptic solution for universal hospital use.

I desire to express my appreciation for the valuable cooperation of Mr. L. C. Pickle, PH.G. and Miss Inez Rausch, R.N. in preparing the solutions and aiding in recording the clinical data herein referred to.

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# IDEALS IN RHINOPLASTIC SURGERY

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THE basic principle upon which my efforts in this field rests is the firm belief that, having in mind the factors that control the processes of growth and repair, one should conduct his surgical procedures to the end that normal functional and anatomical relationship may be established. At the same time due respect must be given to those influences that tend to maintain these relations.

While mechanical principles play an important role in rhinoplastic surgery, it must not be forgotten that we are dealing with living tissues and that permanent results are dependent upon the established laws of biology and physiology.

Those who use bone and cartilage from another human or from one of the lower animals, or who implant ivory, celluloid, vulcanite, etc, for the correction of a depressed nasal deformity, violate these laws, for it is a well-known fact that Nature abhors the presence in the living tissues of any material not nourished by the blood, and that her constant effort is to absorb or expel it. We may be sure that it will be disposed of in time either by absorption, pressure necrosis, traumatism and infection from without, or from the blood stream during the progress of one of the acute infectious diseases, such as influenza.

Chemistry is an exact science. Chemical reactions in the human body are as true to their formulae as in organic or inorganic chemistry under any other circumstances. There is, therefore, no virtue in the claim so often made by the advocates of the use of ivory as an implant, that, because of its near chemical and physical relationship to the tissues of the body, it is better suited for this purpose than any other foreign material.

Even if we assume that an ivory implant will be retained and that its size and shape will remain exactly the same as when it was introduced, the deformity will not remain corrected, for a disproportion is certain to develop between the inanimate implant, which remains constant, and the living tissues by which it is surrounded, which, of course, are subject to changes that occur in all living matter with the passing of the years.

In my opinion any patient who insists upon foreign material as an implant should be apprised of its shortcomings so that he may fully understand the risks that he must necessarily assume when he makes this choice.

The use as a transplant of bone and cartilage from another human or from one of the lower animals has been advocated by some. This procedure, however, does not meet the biologic and physiologic requirements. One would not consider using untyped blood for transfusion; and yet this is an undertaking analogous to bone and cartilage transplantation. It is unnecessary for me to say that the typing of bone and cartilage is impracticable, so we must, in cases where an implant is needed, rely upon tissues removed from the patient's own body, the autogenous transplant.

I have been using bone and cartilage as a transplant for the correction of depressed deformities of the nose for over twenty-five years and some of my oldest patients are still accessible for *x*-ray examination. I feel that the evidence presented by them is irrefutable. Painstaking studies of these cases, made from time to time, show that autogenous bone and cartilage transplants that have been properly introduced and

contacted with live, periosteum-covered bone are not absorbed, that they remain alive and that they take part in the metabolic processes of the tissues by which they are surrounded.

The diversity of opinion concerning the results that I have reported from time to time, I attribute to the unbridled expression of the views of men who are not qualified to speak upon the subject from personal clinical experience. None of these men have ever substantiated their contrary views by the exhibition of clinical findings. Apparently their ideas have been based upon prejudice or upon plagiarized excerpts from medical books that have been handed down from one generation to another.

There are some deformities of the nose due to congenital defects, to faulty development or to traumatic displacement of the parts of the nasal arch, that may be corrected by the use of mechanical appliances or by surgical measures conducted through a small incision in the roof of the nasal vestibule. In the latter instance the instrumentation is controlled by the sense of touch, the fingers of the left hand being kept constantly on the outside of the nose. It is unnecessary for me to say that this procedure demands the co-operation of artistic sense, delicacy of touch and manual dexterity. These qualifications should be co-ordinated by experience.

The difficult art of following with one's fingers concealed instrumentation was well demonstrated in the work of the late Dr. Roe of Rochester, N. Y. Some of Dr. Roe's results were marvellous; his skill was admired by all who knew him; his imitators were many. When most of these men found that they could not secure the same good results, Dr. Roe was accused of withholding some of the important points in his technique. I knew Dr. Roe very well and had the unusual good fortune of being able to do some work with him in Rochester. I can say unreservedly that he had no secrets and he withheld none of the important steps in his technique. Dr. Roe was an artist and he was endowed with remarkable manual dexterity which enabled him to follow with unerring accuracy, by the sense of touch, the course of his instruments under the skin and subcutaneous tissue over the nose. Dr. Roe always contended that only those who were endowed with an artistic sense as well as manual dexterity should engage in rhinoplastic surgery. He rightfully regarded these as God-given attributes that could be cultivated scarcely less readily than one could convert a house-painter into a painter of portraits. That his views have not been accepted, however, is plain when one looks around the professional arena and sees the miscellaneous horde prancing around the rhinoplastic bandwagon in their frantic efforts to get aboard.

Instruments and appliances that exert pressure and counter-pressure from without and within the nose play an important part in replacing and re-arranging the disordered segments of a badly fractured nasal arch. But it must be remembered that these agents are of value and should be used *primarily* only when the patient is seen immediately, or at most only a few days after the nose has been broken.

If we are dealing with an old deformity, the result of a fracture, the situation is different. Here we have conditions that demand special consideration. These are created chiefly by scar tissue, bony union of fragments of the nasal arch in malpositions, nasal obstruction and, last but not least, the elasticity of the skin overlying the nose and cheeks. This elasticity of the skin is one of the most obstinate adverse factors with which we are obliged to contend. The older the fracture with its resulting deformity, the more difficult is the correction likely to be. I have known some of my most strenuous efforts to end in failure and some of my best *primary* results to be destroyed by the slight but unremitting force exerted by the elastic skin, the influence of which is always in favor of re-producing the original deformity. This tendency is always more pronounced in the

young and diminishes as the skin loses its elasticity with advancing years.

There are no set rules by which the malign influence of the skin's elasticity may be overcome. Suffice it to say that at the operation all of the rigid structures of the nasal arch should be mobilized and these should be separated from the overlying skin and subcutaneous tissues by intranasal dissection. It may be necessary, in some cases, to remove offending scar tissue and even parts of the framework, if this is abundant and all of the fragments cannot be jockeyed into position.

The tin-lined copper splint, which suffices in many of these cases to hold the parts in position, should always be kept in place until fixation has occurred, usually in about twelve days. In the young we get bony union in this area in a fortnight, but it is not very firm.

After the removal of the splint, massage, at least once a day, of the skin over the cheeks towards the nose, should be practiced. This should be kept up for several weeks in an effort to counteract the elasticity of the skin.

My experience teaches me that it is only by observing these precautions in some of the old traumatic cases that the primary excellent results, secured by operation, can be made permanent.

Recent fractures attended by deformity, especially if depressed, require the use of the *bridge splint*, which was devised by me many years ago and with which, no doubt, you are familiar. So far I have found no satisfactory substitute for this instrument. When properly applied, it duplicates, as far as is mechanically possible, the developmental forces employed by nature in the process of elevating the flat nose of the infant into the more prominent organ of the adult.

The instrument is best adapted to the treatment of recent severe fractures where there has been considerable displacement of the segments of the nasal arch.

This instrument is useful also in old fractures, especially those attended by depressed deformity. It is necessary in these cases, however, to mobilize thoroughly all of the nasal framework by operative measures before the bridge is applied. In many of these cases too it will be necessary to excise scar tissue so situated that it may interfere with approximation of the broken segments of the arch or where it is suspected that its inevitable contraction may subsequently mar the good results so noticeable immediately after the operation.

Here I feel that it may not be amiss to say that photographs, taken shortly after the operation, seldom show the permanent value of the work done. I have seen photographs of patients thrown upon the screen that indicated excellent results and that called forth vociferous applause from the audience, which still bore on the skin over the nose the imprint of the recently removed splints. Now such evidence as this is of no consequence whatever in the evaluation of final results. Its negative value is recognized at once by those who are experienced in this work. We know full well that within a few weeks or months, under the influence of scar-tissue contraction and the elasticity of the skin many of these fair results will no longer hold.

It is important that we should acknowledge the potency of these adversaries to our skill, which cannot be altogether avoided, in order that we may make allowance in advance for the results.

Open cuts on the nose and face, especially those attended by lacerations and contusions, such as are so frequently seen in injuries due to automobile accidents, call for careful consideration from several points of view. If the injured part has come in contact with the roadway, we may be sure that dirt and carbon from the exhaust pipes of the numerous cars that have passed over the thoroughfare have been ground into the tissues. This material, especially the carbon, which is in the form of a black, impalpable powder, is difficult to remove even under favorable circumstances, but when it is concealed by blood-clots and such antiseptics as iodine and mercurochrome that produce their own discoloration, one may still be left in doubt as to his success even after the most strenuous efforts to eradicate it.

Carbon, retained in the skin and subcutaneous tissues, produces tattoo marks that are very disfiguring; they have the appearance of pencil markings and are permanent unless they can be removed by a plastic operation. The necessary procedure is sometimes difficult and tedious, especially in those cases where it is necessary to make numerous separate incisions. This work is particularly trying when the cartilages of the nose have been cut or macerated and dirt has been included in the scars.

In assuming responsibility for the treatment of primary injuries of this type, one should be reasonably certain that all foreign material has been removed before the severed tissues are approximated or plastic repair is attempted. Law-suits have resulted from an alleged failure to observe the precautions I have noted.

In conclusion I will say that rhinoplastic surgery is indeed a specialty within itself. Many of its operations demand a high degree of manual dexterity, supervised by an artistic sense, without which work in this field does not produce its best results.

It is a specialty that demands great patience and meticulous attention to details on the part of the operator, who should always be frank with his patient and not raise his hopes too high by the promise of perfect results, for the most skillful of surgeons sometimes find that the perfection of their primary achievements are dimmed by the vicissitudes through which each case must pass, owing to two uncertain quantities, namely cicatricial contraction and the elasticity of the skin.

It is essential therefore, for those unfamiliar with rhinoplastic methods and their limitations and for those who are not personally interested in this department of surgery, to beware lest they be misled by the brilliant results so often depicted by novices in this field, especially those who take photographs of their patients immediately after the removal of the molding copper splint and tacitly attribute permanency to the results.

The copper splint, which I devised a number of years ago, will deliver a perfect primary result if the framework of the nose has been thoroughly mobilized, but this improvement will be fleeting unless the proper preliminary operative technique has been employed and unless the proper after-treatment is rigorously carried out.

## SUMMARY

1. In rhinoplastic surgery the fundamental consideration should be to establish normal *anatomical* and *functional* relationship and to foster those influences that tend to maintain these relations.

2. All procedures must conform to the laws of *biology* and *physiology*. Therefore the introduction into the living tissues, as implants, of any foreign material incapable of being nourished by the blood of the individual, is to be condemned, for such substances will eventually be expelled or absorbed. Any patient who insists upon their use should be warned beforehand.

3. Autogenous *bone* and *cartilage* from the rib, introduced as first suggested by me are the only tissues suitable for implantation into the nose for the correction of a depressed deformity.

4. Bone, when properly contacted with live, periosteum-covered bone, remains alive and participates in the metabolic processes of the tissues in which it is imbedded; its growth is in proportion to the stress placed upon it.

5. The Carter bridge splint is the best appliance for the treatment of recent severe fractures of the nose and for some old traumatic deformities after they have been mobilized.

6. Photographs, taken shortly after operation, should not always be considered evidence of a permanent successful outcome.

7. Open wounds, especially those due to automobile accidents, should be carefully inspected for the presence of carbon and other foreign matter. If such substances remain in the tissues they will produce very objectionable tattoo marks.

8. Rhinoplasty is a specialty within itself. It demands artistic endowment, manual dexterity, patience and careful attention to every detail in operative procedures and the after treatment.

# GRAFTS AND TRANSPLANTS

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A GREAT deal has been written concerning the grafting of tissues and, occasionally, of entire parts of the body. However, so much of this information is of a controversial nature from a biological point of view, it may be appropriate to review some of the more recent facts obtained from experimental studies upon this subject, so that a clearer understanding of what constitutes a graft may be obtained. Further, it is proposed to discuss the use of transplants, other than grafts, and what success may be expected in their use. In this way the subject may be clarified.

Part of this misunderstanding is due to the indiscriminate use of the terms "graft" and "transplant" as words of common meaning. They are not synonymous, for the definition given in any standard dictionary specifies that a graft is the transplantation of living tissue from one individual to another or from one part of the body to another part of the same individual, with the expectation of that tissue living in its new environment. To graft we must transplant, but the act of transplantation does not necessarily imply that the tissue is expected to remain alive in its new environment. It is unfortunate that these terms should have been employed so loosely for, as their meanings are quite different, it leads to confusion.

The success of grafting of tissue is dependent upon two important factors; first, the compatability between the grafted tissue and that into or onto which the transplant is made and, secondly, the ability of the graft to obtain nourishment so that it may remain viable until healing is completed.

Let us first discuss the second of these assertions. The cells of the body do not obtain their pabulum directly from the blood vessels. Between the vessels and the cells "there intervenes a space of varying dimensions containing a fluid, the lymph, whose composition is very similar to that of the blood minus its red corpuscles. . . . "[1] Each cell of a tissue, in other words, is bathed in lymph from which, by means of osmosis, it obtains its nutrition and, in like manner, gives up the end-products of its catabolism. In vascular tissues the dimensions of the tissue spaces are small, there is but little distance between the capillary and the cell; in less vascular tissues the spaces are of greater dimensions and the cell is not in as close proximity to the capillary. Tendons and bones are examples of this type. Finally, there is a type of tissue in which the tissue mass is avascular and the nutrient lymph for the cells is obtained, through imbibition, from a vascular plexus which surrounds the periphery of the mass. Here the cell is far distant from its capillary. The life of each one of the cells is dependent upon the juice or lymph in its tissue spaces as in the other types of tissue, but in this case the lymph is obtained from the capillaries surrounding the tissue mass or abutting upon one of its surfaces. This type of tissue is known as vegetative (having the power to grow like a plant). Hyaline cartilage, the cornea and the epithelial layers of the skin are true vegetative tissues.

From a theoretical consideration it may be said that the less vascular the tissue, the larger are the dimensions of the tissue spaces and, consequently, the greater is the distance between the cell and its vessel which supplies it with nourishment through the lymph in the spaces. It is supposed,

therefore, and I think correctly, that the less vascular the tissue that is transplanted, the greater is the chance for a successful graft. However, in tissues other than those of the vegetative type, the size of the transplant must of necessity be very minute to live by imbibition alone.

The reason that transplantation of vegetative tissue as a graft is so often successful is that the mass of tissue is not in any way dependent upon an intrinsic blood supply for its nutrition during the healing process. This type of tissue absorbs plasma from the surfaces of the wound with which it is in contact and, through its power of imbibition, it obtains from its periphery the necessary pabulum to keep its cellular elements viable. It is the tissue spaces that carry the nutrient lymph from the periphery of the mass to each cell and, consequently, there is no need for an adjustment of the vascular circulation of the transplant to that of the surrounding tissue, to reestablish its nutrition.

The power of cartilage to live when merely surrounded by lymph is clinically demonstrated through the finding of cartilaginous loose bodies within the knee-joint. These masses are alive, for microscopic section shows normally staining cartilage cells. Small masses of autogenous cartilage have been placed in the joints of dogs and have been shown to have remained viable for a period of time of at least thirty days' duration, though entirely loose within the synovial sac.[2]

For success in the grafting of tissue of the vegetative type, however, the mass must not be so great in size that it is unable to absorb sufficient nutrient lymph from the circulation of the tissues into which it is transplanted; otherwise death of the more distant cells occurs, leaving merely the matrix of the tissue. The size of the transplant must therefore be limited to the amount of circulation that is present in its new environment.

Transplantation of masses of tissue, which are not vegetative in type, invariably fails in producing successful grafts. Here the tissue mass contains blood vessels and the circulation within these vessels is cut off at the time that the transplant is excised and, before it can be reestablished, the cellular elements of the tissue have perished from lack of nourishment and the transplant becomes merely a dead, inert mass made up of the reticulum of the tissue that was transplanted, a skeleton or framework of the former structure. If it be bone, it is merely the calcified stroma, for the lacunae contain no cells and the vascular channels no vessels or connective tissue. If fascia, the fibers are all that remain, for the cells have disappeared. As these tissues are non-vegetative in type, they contain their own network of vessels from which the tissue spaces obtain the lymph to nourish the cells. Consequently, these spaces are of small dimension, merely extending to the capillaries within the tissue, and do not open upon the periphery of the mass as do those of masses of tissue of the vegetative type.

Theoretically, a transplant of minute size, though it is removed from tissue which is dependent upon an intrinsic circulation, may remain alive. For if the transplant is so small that the plasma from the wound which surrounds it can seep through all its tissue spaces and thereby reach each cell, the transplanted tissue should remain viable and would be a graft.

The thyroid glands of rats and guinea pigs have been transplanted by Loeb[3] who found, if autogenous in type, that a few of the peripheral cells of the transplant remained alive, while those in the center of the mass necrosed, were absorbed and were replaced by fibrous connective tissue which was formed through the ingrowth of vessels from the surrounding tissue.

If a massive autogenous transplant of the non-vegetative type is surgically clean, it may be retained in the body, causing but slight reaction to the surrounding tissues. In time the periphery of the foreign body, for that is what it really is, becomes eroded through the activity of the granulation tissue which forms upon the surfaces of the wound which surrounds

it. In many places this tissue penetrates into the mass, revascularizes it and absorbs the structure of the old stroma, replacing it with new and, in so doing, may use both the organic and inorganic materials of which it is formed.

In bone transplants the formation of new bone depends on the resorption of the transplant. [Leriche and Policard.[4]]

In man, a fragment of bone transplanted into another bone always dies. At the present time this fact is a certainty. Its nutrition is no longer assured after its transport into the tissue of the host. . . .

Soon the connective tissues of the host penetrate into the cavities of the transplant, rehabilitate it progressively, and erode its bone substance which, little by little, is rarefied at the same rate that it is rehabilitated by the connective tissue. From this there results automatically the freeing of calcareous materials which soon bring about in the surrounding connective and interstitial spaces the formation of new bone. All this transpires according to the general laws of ossification. [Leriche and Policard.[5]]

In experimenting with autogenous fascia in dogs it has been shown that the strips of fascia first become revascularized at their margins by the ingrowth of capillaries from the vessels which surround them, to be followed in some cases by the replacement of their tissues. In contradistinction to this, an inert substance such as kangaroo tendon becomes encysted and is slowly absorbed. [Horsley.[6]]

In the use of large, full-thickness grafts of skin, the so-called Wolfe-Krause, the epidermis or true skin remains viable, though the more superficial layers are usually cast off, while the corium, the mesoblastic layer dies. The cells in this layer degenerate, leaving behind the fibrous tissue stroma. New blood vessels from the tissues of the host grow into this layer, a round cell infiltration occurs, the old stroma is absorbed and becomes replaced with new connective tissue. During the period in which resorption and replacement is occurring in the corium, the cells of the epidermis remain alive, through the imbibition of nutrient lymph, until a new circulation is established in the corium. [Davis.[7]]

The sooner a transplant of this type is vascularized, the sooner it becomes replaced. Not only are the old vascular canals of the transplant used for revascularization, but new openings are made into the substance of the transplant, through erosion by the capillaries from the surface of the wound. This type of transplant cannot be called a graft, it does not live. It may, however, act as a scaffolding into which the vessels grow from the surrounding tissue in which it lies. These absorb the dead elements and replace them with live ones. But, unfortunately, this does not always occur, for the stroma of the transplant may entirely disappear through absorption or it may be replaced by an entirely new type of tissue. We do not know the reason for this. It may be due to vascular changes, to the lack of need for that particular type of tissue in that particular part of the body, or to some local condition.

Following the transplantation of fascia lata to fill a defect in an artery, the transplanted tissue becomes resorbed and replaced by the normal structure of the vessel wall. Fascia lata transplanted into a defect of the urinary bladder is invariably replaced by connective tissue containing true osseous tissue.[3]

If it were possible to immediately reestablish the circulation within the mass of tissue by means of suture of the vessels, the transplant might succeed as a graft. A few reports of cases, where this has been accomplished, have been published. If the transplant is an organ, however, it would seem to be necessary to reestablish its nerve supply as well before it could function. This is a more difficult problem than that of preserving the circulation. From the facts at hand, it seems that the more specialized the cells of the transplant the less chance there is for normal function, even though the graft is successful. It is quite evident, therefore, that masses of nonvegetative tissue have not the histological structure to lend themselves as grafts, though they may be of use in replacing needed tissue, by being transplanted with the expectation of their

absorption and replacement with like tissue.

Let us now consider the question of compatability between the tissue of the graft and that of the body into which it is transplanted. Any surgeon who has had experience in skin-grafting and has used homologous grafts (that is a graft from another individual), has had the sad experience of seeing the graft either fail to live or, after thriving for a week or so, suddenly disappear over night without any apparent cause. In this instance the grafted tissue is absorbed by the body of the host. It was thought at one time that the reason for this failure was that the blood of the two individuals, the donor and the recipient, were of different groupings. For a time, therefore, when homologous grafting was contemplated, we chose an individual as donor of the graft whose blood was of the same group as that of the individual who was to be grafted. Here again failures occurred. Now, as far as the question of skin-grafting is concerned, no surgeon would think of using homologous grafts.

Loeb[3] has shown by experiments upon animals, transplanting from one to another, that the length of time that a graft remains viable depends upon the quality of the leucocytic and fibroblastic reaction that occurs toward the graft in the recipient. That the intensity of the reaction depends upon the nearness of blood relationship between the donor and the recipient, as less reaction occurred where this was close than where there was none, and that the further one departed from this relationship the greater was the amount of fibrocellular reaction. The reaction was more severe when the transplant came from an individual of another race and was most severe when heterogenous transplants (from an animal of a different species) were used.

Padgett[9] applied this information to his clinical work in skin-grafting. He found that an immediate "take" occurred in the majority of cases where homologous grafts were used. That if the individuals were not of blood relationship the transplanted skin faded away between the second and fourth week. Where there was blood relationship the transplant did not disappear as soon but, even in the case of child and parent, it eventually did become absorbed. The only cases where homologous grafts were successful were where the donor and recipient were homologous or "like" twins.

From the experimental work that has been done, it is thought that this reaction in homologous grafting is caused by primary substances that are given off by the transplant which act as a toxin that stimulates the cells of the recipient to a leucocytic and fibroblastic cellular reaction against the graft. These substances do not appear to act in the nature of antigens and, therefore, do not produce immune substances in the host.

There is evidence that the same type of irritation is produced in the tissue of the host by transplants of the non-vegetative type. For it has been observed by us, when homologous fascia strips have been used in the repair of hernias, that the wound reaction during healing has been more severe than when autogenous fascia was employed. There was more induration, often the skin edges showed signs of irritation and, in some cases, the wound broke down though not infected.

Homologous transplants of bone have produced the same type of reaction in the tissues of the recipient, and heterogenous transplants have caused so great a reaction that the wounds of the recipient have failed to heal and the transplants have been extruded.

## SUMMARY

The transplanting of tissues as grafts as well as where replacement may be expected plays an important part in the operative procedures of today. The surgeon, however, should discriminate in his conversation and writings between the terms "transplant" and "graft," for as we have seen, they are not synonymous

words and, as educated men we should use correct English.

A graft is an immediate transplantation of tissue which continues to live and grow in its new environment. For a graft to be successful, the cells of the transplanted tissue must obtain nutritious lymph during the period of healing. The only tissues that have been found to be successful for grafting, because of their structure, are those of the vegetative type, that is those which have no intrinsic blood supply.

Tissues which contain intrinsic blood supplies are not suitable as grafts, as the circulation of blood within them becomes interrupted during the act of transplantation and, before it can be reestablished, the cells die for lack of nourishment and all that remains is the stroma of the tissue. This, however, may be revascularized from the tissue surrounding the transplant and is resorbed and often replaced by tissue of identical structure. The transplantation of tissue of this type is a useful procedure to supply losses, but it must not be confused with the act of grafting nor should such a transplant be called a graft.

Transplants of any tissue should, if possible, be autogenous in type, that is composed of tissue from the same individual. If foreign tissue is transplanted in the body of an individual it produces, through its irritating action, a leucocytic and fibroblastic reaction in the tissue of the host, which may result in the total destruction and absorption of the transplant and its replacement with fibrous tissue, or its extrusion from the wound. Experience has demonstrated that heterogenous and homologous grafting results in failure.

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# FORENSIC MEDICINE

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## CHANGING OF FINGERPRINTS

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SOME forty years ago Mark Twain in writing his famous book entitled, "Pudd'nhead Wilson," had Lawyer Wilson in his final address to the jury say:

> Every human being carries with him from his cradle to his grave, certain physical marks which do not change their character, and by which he can always be identified—and that without shade of doubt or question. These marks are his signature, his physiological autograph, so to speak, and this autograph cannot be counterfeited, nor can he disguise it or hide it away, nor can it become illegible by the wear and mutations of time.
>
> This autograph consists of the delicate lines or corrugations with which Nature marks the insides of the hands and the soles of the feet. These dainty curving lines lie close together, like those that indicate the borders of oceans in maps, and they form various clearly defined patterns, such as arches, circles, long curves, whorls, etc., and these patterns differ on the different fingers.

Mark Twain did not claim this as an original discovery, but his book brought the idea to the public so that this has been an accepted theory, fostered by many scientific works and proved by millions of fingerprint records.

In Chicago in 1933 the "Handsome Jack Klutas" case raised a new question of the possibility of changing finger prints and facial contours so as to defeat the aims of justice by making identification difficult.

While the public believes in the possibilities of miracles performed by plastic surgery, certain essential points must be made clear before further discussion.

Skin grafts taken from one person and transplanted to another or taken from animals and transferred to humans are so seldom successful that they may be eliminated from consideration. Where the very rare case has been successful at first, ultimately the graft was replaced by scar tissue. Ordinary skin taken from other parts of the body, with the exception of the palms of the hands and the soles of the feet, does not contain the characteristic ridges and will not develop them on transplantation.

If we can change one fingerprint we have changed the fingerprint classification. Certain areas of the palm and the sole contain such characteristic ridges as are found on the finger tips but not of the same grouping.

A recent inquiry from the California Bureau of Identification regarding the possibilities of changing finger prints prompts the mentioning of a case:

> The patient, a man, has been under my care for the past two years for reconstruction of his burned hands. The distal phalanx of the right forefinger was markedly flattened and the finger contracted. To build up the flattened end and make a new touch pad I decided to place a skin graft from the palm in addition to releasing the scar tissue causing the contraction. An area on the palm was selected for its skin ridge markings similarity and in order to better demonstrate the result the skin was turned around.

As far as I know this is the first reported and authenticated instance of change of finger prints by surgery (Fig. 1). The ridges do not appear completely for several months after transplantation and one should not

be misled on seeing an early graft.

If only plain impression prints are made the scars if present will not show. A complete roll print however will show the incision lines in certain cases, especially if recently made. The fact that the ordinary latent print is a plain impression print, makes this of special interest.

It would be possible to repeat the change, especially if it were a case of covering or eliminating old prints on file. The simplest way would be to remove the skin and graft from some other part of the body, as many finger tips in manual labor types, show no ridges.

Detection of such a subterfuge would entail the recognization of scars on the finger. If ridges were present in the suspected grafted area, inspection of the palms and soles with the tell-tale scars would be sufficient evidence. If no ridges are present on the suspected fingers, the entire body, usually the thighs, would furnish evidence of areas having supplied the graft tissue.

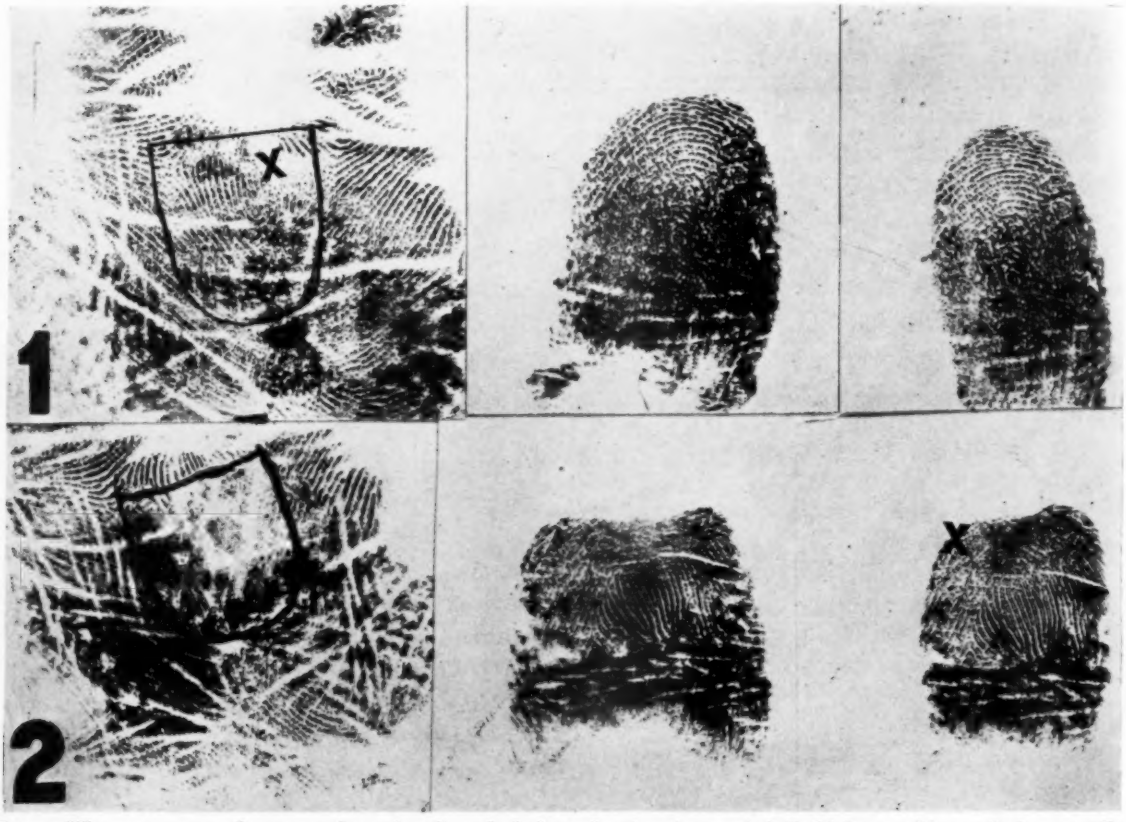


Fig. 1. The upper row shows a palm print directly below the ring finger. A full thickness skin graft from outlined area (X) was interchanged with a full thickness graft from the right forefinger. The prints (roll and plain) of right forefinger before interchange are also shown in top row.

In the lower row (2), the palm area is beginning to show the ridges of the forefinger skin which has been transplanted up side down. The roll print (middle lower) shows the transferred ridges plainly and at the bottom of the print the scar is barely discernible. The plain print marked (X) shows the looped ridges of the graft from the palm, which has also been turned around.

All prints were made by and through the courtesy of Captain Howard Barlow and M. Gaskell of the Los Angeles County Bureau of Identification.

If fingerprint classification is not to mean identification we must realize that the criminal who is smart enough to have his fingerprints altered is going to have other surgical aid. Plastic surgery is being utilized to defeat justice by changing facial contours, removing scars, etc.

When we have a national act requiring universal identification measures we must have not only fingerprints, but prints of the palms and soles as well. Added to this must be an up-to-date understanding of plastic surgery possibilities.

# HEAD INJURIES

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HEAD injuries give rise to two kinds of symptoms: the immediate and remote. Both, however, are usually due to the occurrence of trauma sufficient to produce the acute and subsequent manifestations. Skull fracture, blood in the spinal fluid, orificial bleeding, focal cerebral palsies, convulsions occurring after the injury, prolonged unconsciousness, ventricular distortion, and vomiting following the injury, are both the absolute and presumptive criteria, that the trauma sustained is responsible for the symptoms the patient presents.[1]

Skull fractures are important in so far as they affect the intracranial contents, either the brain, its membrane or vessels.[2] Fractures are of immediate moment only when depressed, yet the intracranial contents may be seriously involved without any evidence of fracture or any external evidences of injury.

Always it is the surgeon who is first confronted with the acute head injuries, and wherever indications of a threatened sepsis occur, it is his duty to prevent or cure it, and where manifestations of compression occur, his duty is to relieve it. Compound fractures, brain laceration, dural tears, fractures that communicate with the paranasal sinuses and mastoid sinuses are open routes through which infection may enter. Should meningitis develop as a result, it will do so within forty-eight hours to a few days after the injury has been sustained. There is great danger of brain abscess in the areas that lie immediately beneath the compound skull fracture, and for this reason, a compound fracture must be converted into a simple fracture as soon as possible by thorough cleansing of the wound, the removal of all loose fragments of bone, complete excision of devitalized tissue, the elevation of any bony depression that may be present and closure of the wound. Even the elevation of depressed bone should be deferred until one is reasonably sure that the patient's condition permits, for the danger of premature intervention is at times as great as the injury sustained.

Fractures that pass through the nasal sinuses may give rise to pneumocephalus,[3] a rare complication, but an extremely dangerous one, for the dura, in such cases, is always torn. The air makes its entrance into the brain through the subarachnoid or the subdural space. Thus, a fracture which may appear to be but linear is actually compound, for it has a direct communication with the external air within the nose. Such accumulations of air make their way into the lateral ventricles and *x*-rays will often present definite evidences of self-induced ventriculograms. The mucous membrane of the nose grows into the dural rent and the patient makes a so-called spontaneous recovery. However, after a variable length of time, a nasal infection occurs and extends from the nose into the dura and arachnoid by transmission of the infection by direct tissue continuity, which eventually gives rise to a meningitis, frontal abscess and death. The early recognition of such condition in the absence of infection, providing the patient's condition allows, should be treated by opening the sinus and transplanting a layer of fascia lata or skin, to obliterate the contact existing between the nose and the pia-arachnoid.[4] Where the cribriform plate is fractured, as a rule, these sequelae do not follow unless the bone fragments are widely separated or the bone itself penetrates the dura. The reason for this is that

the bone and dura in this region are one structure and cannot be separated, and the epithelium lining is of a highly specialized character and does not proliferate as rapidly as the rest of the nasal mucous membrane.

Fractures in the frontal region may extend through the cavernous sinus, and though rare, present at times a murmur audible both to the patient and physician, in addition to a unilateral exophthalmos, conjunctival edema, and an obliteration of the disc margins. The bruit may be present with or without the ocular manifestations and for this reason skull auscultation should never be omitted in frontal region fractures.

The most vital issue in the management of those cases, that present no evidence of destructive injury, are those that manifest signs of impending increase in the intracranial tension. The latter is caused by edema of the brain, intracranial hemorrhage or both. The natural intracranial regulatory mechanism will often successfully control such increased pressure without recourse to surgical or medical assistance. What are the signs that indicate a disturbance in this regulatory mechanism, what are the danger points and when is interference justified?

The most important of all signs is the state of consciousness. Where unconsciousness supervenes, the intracranial regulatory mechanism has ceased to function and the rising intracranial pressure is no longer under control. On the other hand should consciousness return, it would indicate a diminution of the intracranial tension. The deeper the coma, the worse is the outlook.

Emotional disturbances, irrationality, marked restlessness are signs that should make one aware of an impending coma. Dandy states that "to subdue such restlessness with morphine is as hazardous as masking pain in abdominal lesions."

Due to the unconsciousness of the patients immediately following head injuries, examination of the eyes is a peculiarly valuable procedure. It is then that the pupillary phenomena are of considerable importance. Such pupillary phenomena must be observed frequently, for often the state of the pupil will vary, even at hourly intervals. Fixed dilated pupils and a suppression of the deep tendon reflexes offer a serious prognosis. A unilateral dilated fixed pupil is indicative of an epidural or subdural hemorrhage. Inequality of the pupils is usually due to cortical irritation or cortical pressure rather than involvement of the third nerve itself.[5] However, one must be certain that the pupillary disturbance is not due to local changes, so that such findings will not be attributed to intracranial involvement. An example of such error is very well illustrated in the following case.*

Case 1. E. B., a boy of fourteen, while skating, tripped and fell forward on his head. He sustained two lacerations of the forehead and was unconscious for a very short period before being brought to the hospital. The wounds were sutured and *x*-ray revealed no evidence of skull fracture. A routine spinal fluid examination was negative and aside from the lacerations the general and neurologic investigation revealed nothing abnormal. The following day the patient complained of headache, and the resident upon examination found a stiffness of the neck, a suspicious Kernig reaction, the right pupil markedly dilated, both reacting poorly to light and in accommodation with a normal pulse and temperature. A diagnosis of a meningeal hemorrhage was made but after questioning the interne staff and the nursing staff, it was discovered that one of the internes had instilled homatropin in the eyes the night before, in order to examine the fundi. The cause of the pupillary findings determined, it was also agreed that the neck and back stiffness was probably due to the trauma of the spinal puncture, which was performed with difficulty. After a short stay and further observation, the patient was discharged with no abnormality in his physical findings.

Irregularity both in the rhythm and rate of the pulse is another sign of an

* Cases cited in this paper are from The Metropolitan, Flower and Polyclinic Hospitals.

impending disturbance in the intracranial regulatory mechanism. The same may be said of respiration. A persistent rise in the systolic blood pressure with a concomittant fall in the diastolic pressure is an ominous sign.

Following serious injuries of the head, and particularly in those cases that are manifesting some signs of increasing intracranial tension, frequent and regular rectal temperature readings become necessary, for a persistent rise in temperature is a warning that the intracranial pressure is nearing or has passed its margin of safety.

There are some who advocate and others who condemn the use of lumbar puncture either as a diagnostic or therapuetic procedure. There is no doubt that in many cases it facilitates a diagnosis, and prevents one from groping in the dark, but is one justified in utilizing it as a therapeutic aid in the presence of evidence of intracranial bleeding, whether epidural, subdural, or cerebral? Of these, the epidural hemorrhage is one of the grave complications that offers the best prognosis, if recognized and properly treated. The recognition, however, must be early and the treatment, to reiterate, proper.

Should an epidural hemorrhage take place following a head injury, the symptoms as a rule follow rather rapidly. After a brief initial period of unconsciousness, the patient may appear entirely well or he may be sent home from the hospital because there are no signs or symptoms of any injury. A short period thereafter, however, an insidious drowsiness takes place, often with an associated motor weakness on the side opposite the injury, which makes its appearance at first in the face, then in the arm, and which may or may not extend to the leg. This may or may not be associated with convulsive seizures, which usually traverse the same course as the motor weakness. The entire syndrome becomes profound and death may be the inevitable outcome of this epidural hemorrhage. On the other hand spontaneous recovery can take place with or without the occurrence of epileptic seizures in the future.

The middle meningeal artery in its upper part is adherent to the dura, and in its lower part is within the bone. Should a tear occur in its wall, retraction therefore can not take place and a slow, uncontrollable hemorrhage ensues. After a variable period of time, an extradural clot occurs which gives rise to an increased cerebral compression.

What effect will lumbar puncture have in such a case? There may be an immediate and temporary alleviation in the signs and symptoms the patient presents, but if the intracranial tension is high, this alleviation soon gives way to aggravation of the initial picture. By relieving the intracranial tension through the lumbar route, pressure is removed from the bleeding dural vessel, and the hemorrhage continues again. With every repetition of the lumbar tap there is an additional stripping and injury to the dural vessel, with a subsequent and inevitable continued bleeding.

Whether the use of hypertonic solutions intravenously has a similar mechanical effect is a moot question. If the use of drugs or intravenous glucose solution does definitely reduce the intracranial pressure, its effect in the presence of slow bleeding would be no different from that of lumbar puncture, and as such should be judiciously employed and with the greatest caution, if at all. Those patients who will get well, will get well without these procedures, and it is doubtful if they will be of any value to those patients who will not. It is best to adopt a policy of ultra-conservatism until it becomes absolutely necessary to interfere, for 70 per cent of these patients will recover spontaneously if left alone.[2] When indications definitely determine that the margin of safety has passed, a subtemporal decompression and control of the bleeding points will prove a life-saving procedure in 10 per cent of these cases. Those who

die within the first few hours after their injury, fall into the remaining helpless category, in which no method whatever would change the fatal outcome.

Those cases commonly designated as suffering from concussion, are actually caused by multiple punctate hemorrhages into the perivascular spaces of the brain.[6–8]

Where the hemorrhages are more extensive the condition may no longer be called concussion. The punctate hemorrhages of themselves never give rise to increased cerebral compression, but the perifocal areas of edema incident to them may at times do so. Although death does not occur in the average case of concussion, in the more extensive ones it may, particularly in those in whom unconsciousness is profound. For these cases the administration of caffeine-sodium benzoate in doses of 7½ grains, intravenously or intramuscularly, will effect a reduction in the intracranial pressure as measured by the spinal manometer, anywhere from 20 to 50 mm. within three minutes after the injection. This reduction will be sustained for a period of forty-five minutes or more and may be repeated every two or three hours.[9] In the intervals between injections hypertonic dextrose solution may be administered by vein, in 100 c.c. doses of a 50 per cent solution, as often as three times a day. Rectal instillations of a 25 per cent dextrose solution in 100 c.c. doses are given every three to four hours, and lumbar puncture may be resorted to if a diagnosis of concussion with an increasing intracranial tension has been ascertained. With these procedures, we now attempt to re-establish the normal intracranial regulatory mechanisms.

Frequently individuals who have been the victims of a skull injury, with or without a period of unconsciousness, and with or without evidences of meningeal bleeding or skull fracture, will present a symptom complex variously designated as a post-traumatic state or neurosis. These are really the cases that offer the greatest problem both from a medicolegal and medicosurgical standpoint. The signs and symptoms often resemble those from a generalized cerebral arteriosclerosis and present encephalographic results that are no different from the encephalographic findings in degenerative diseases of the brain or idiopathic epilepsy.[10]

Headache is the most frequent, the most obstinate and often the most troublesome of the remote symptoms. It usually is accompanied by a distressing dizziness, and it is often difficult to determine whether the headache is truly a post-traumatic one or one that is purely neurotic in character. Those patients who really suffer from true post-traumatic headaches always complain of the fact that these headaches occur in the same location. They are always accompanied by a specific type of dizziness and last for a few minutes, occurring any time of the day, and worse at a given specified time.[11] In contradistinction, the neurotic headache varies greatly in location, occurs in attacks lasting a few hours or is continuous in its duration. The headaches are usually associated with nervousness, general body pains and mental disturbances such as excess fatigue, insomnia, gastrointestinal symptoms, and a complex conglomeration of complaints, which frustrate any attempt to arrive at a definite conclusion. These headaches may last for years and may never disappear. In a number of cases spinal insufflation of air is the only means whereby this most annoying complication can be abolished, providing the headaches are organic in nature.

Frequently patients who have sustained a head injury will present the symptom complex commonly known as "punch-drunk." Although there are some investigators who are averse to the recognition of traumatic encephalitis, the work of Asnato and Gilberti[12,13] lends credence to the fact that traumatic encephalitis is a definite entity. The following cases will help to illustrate this to an even more marked degree:

Case II. P. B., a man thirty-two years of age, whose past and personal history were entirely irrelevant, sustained a head injury while in a football game, seven years ago. There were no evidences of fracture or intracranial hemorrhage of any kind. The patient was unconscious when taken off the playing field, but six hours later, developed a right spasmodic torticollis. This condition was thought to be functional in nature and the patient was treated accordingly. However, all methods of psychotherapy apparently failed to be of any beneficence. The patient at some time later was placed in a cast and at another date was subjected to a cervical sympathectomy without any relief of symptoms. Soon there appeared a gradual fixity of his facies and as time went on, three years after the head injury, the patient manifested all the signs of a fully developed parkinsonian syndrome, identical with those cases seen following epidemic encephalitis. There is little doubt that this is a case of traumatic encephalitis, the trauma of which may or may not have precipitated an existing latent infectious encephalitis.

Case III. J. D., a man, thirty-seven years of age, whose past and personal history were entirely irrelevant, two years ago sustained a skull fracture in the left temporoparietal region when he was struck by part of a falling brick wall. "He was never right since that injury." Two years later, he presented the following: There was a definite slowing of all the voluntary activities the patient attempted and a loss of the normal associated movements of the arms in walking and an unmistakable mask-like facies. There was a coarse lateral tremor of the head particularly on concentration. There was a narrowing of the left palpebral fissure; the left pupil was definitely larger than the right and reacted poorly both to light and in accommodation. There was a narrowing of the right nasolabial fold and the tongue deviated somewhat to the right. There was a marked coarse tremor of the outstretched arms, and both presented a cog-wheel phenomenon which was also present in the legs. There was a slight ataxia in the finger to nose test greater on the left than on the right. The blood and spinal fluid Wassermann reaction was negative. This patient presented unmistakable evidence of an incipient parkinsonism, undoubtedly the result of the head injury originally sustained.

Dizziness is a distressing sequel of head injuries and is a subjective complaint that arouses considerable controversy, particularly from the medicolegal aspect. The type of dizziness the patient may describe will often bear little weight in the face of medicolegal testimony. For this reason every patient who complains of post-traumatic dizziness should be given the benefit of the established vestibular tests by a competent otologist. Any and every abnormal response should be noted in order to indict a brain or peripheral eighth nerve lesion as the pathologic cause of the vertigo so that the subjective dizziness now has objective confirmation. On the other hand, vestibular tests may demonstrate an intracranial lesion, yet the patient may not complain of dizziness at all.[14]

Neurologically there may be definite evidences of focal signs and symptoms, and yet there may be no confirmatory proof clinically, in spite of the existence of post-traumatic brain pathology. Frequently, however, definite organic changes can be demonstrated in many patients who have been subjected to encephalography, and at times this remains the only means at our disposal whereby the organic and functional syndromes can be satisfactorily differentiated. Abnormal ventricular dilatation, excessive accumulations of air over the convexities of the brain, a pulling of either ventricle toward the site of the injury, obliteration of the normal contour of the ventricles, are the abnormal aberrations that give proof that cerebral injuries have been positively sustained.

Epilepsy is probably the most harassing of all the post-traumatic sequelae. They may be true epileptic seizures, focal epilepsy and functional in their manifestations. These may occur with or without fractures of the skull, and the true epilepsy is usually due to brain scarring or occurs in those individuals in whom meningeal bleeding had taken place after the injury. It is at times most difficult to distinguish between the true and the

hystero-epilepsy, in which case encephalographic studies may help, not only in the diagnosis but also in the relief of the seizures. One must be definitely certain, however, that the patient had not been an epileptic prior to the head injury in order to avoid confusion both as to diagnosis and therapy to be adopted.

Patients may manifest partial aphasia or complete aphasia, in the motor or sensory sphere, or in both. These complications may exist with and without skull fracture. These aphasic phenomena occur immediately or soon after the trauma and may last for a period of years, improving when they do, to a variable degree. In others the aphasia remains permanent.

Case IV. A. Z., a man forty years of age, was struck over the head in a hold up. He was unconscious but there was no evidence of skull fracture. On regaining consciousness he presented a right flaccid hemiplegia and a motor and sensory aphasia. Four years later a craniotomy was performed over the left frontoparietal area, an extradural blood clot was removed, but the patient still presents a right-sided flaccid hemiplegia and a partial motor aphasia.

Case V. S. D., forty-five years of age, sustained a head injury in an automobile accident ten years ago, which resulted in a right-sided hemiplegia and a complete motor aphasia. Five years after the injury he was subjected to a left-side craniotomy following which the aphasia disappeared, though the hemiplegia persisted.

From these 2 cases it would seem that surgery offers some hope in this condition, even in cases of long duration and in those that would appear to be in an apparently hopeless state.

Following adequate head trauma, psychic disturbances will often ensue. They may be of a short duration or may last for some time after the injury. Although basal fractures give rise to the greatest number of mental disturbances, similar complications may occur without any evidence of meningeal bleeding or fracture of the skull. As an example:

Case VI. E. W., a man of twenty-eight, whose past, personal and family history was irrelevant, while employed in the capacity of tree cutting for the C.W.A., was struck on the head by a falling tree. He was rendered unconscious as a result. *X*-ray of the skull was negative and so was the examination of the spinal fluid. He was irrational immediately after and during his stay in the hospital and had to be restrained. Following this he became depressed and presented a picture which was very much akin to the depressed state of a manic-depressive psychosis. He attempted suicide by cutting both wrists with a razor, but was unsuccessful in his attempt. He was institutionalized for a period of three months, following which he had made a gradual recovery.

Case VII. C. D., a man thirty-six years of age, whose past, personal and family history was irrelevant, fell one floor from an elevator shaft and in doing so sustained a head injury. All examinations proved negative. A short time after the accident the patient presented various behavioristic disturbances. He became depressed, would wander away from home, and once after a disappearance was found drowned, undoubtedly as a result of suicide.

Thus, definite psychopathic personality changes may take place following any type of head injury, and mental changes are naturally more prevalent in the severer ones. Memory defects and changes in the disposition of the injured will often be noted. Patients who were previously quiet and reserved, appear irritable, boisterous, show undue fatigue, retardation of thought, and some persons become extremely susceptible to alcohol as a result. Kasanin[15] presented 15 cases in children with personality changes following trauma. Thirteen of these were regarded as psychopathic, having first been treated as functional cases with prolonged and unavailing psychotherapy and social study.

Severe injury of the brain interferes with the formation of the proper inhibitory influences in the integration of one's personality. The outlook in the posttraumatic patients is more favorable than in the cases of behavior disorders due to other causes. More exhaustive encephalo-

graphic studies should be made in these cases and where psychotherapeutic measures fail these people should receive prolonged and intensive training in properly supervised correctional institutions.

Where there is no history of trauma, in cases of subarachnoid hemorrhage, with or without evidence of skull fracture, it is at times almost impossible to determine whether the trauma was productive of the subarachnoid hemorrhage or whether the unconsciousness ushered in by the subarachnoid bleeding was the cause of the head trauma such patients often sustain. If the history reveals the occurrence of similar bleeding on a previous occasion, one may be reasonably sure that any evidence of skull injury present must have been incurred during the period when consciousness was lost. So-called "idiopathic" subarachnoid hemorrhages are usually due to mycotic aneurysms of the smaller cerebral vessels and are caused by a weakening of the medial coat of the vessels, particularly at their points of bifurcation. Spontaneous subarachnoid bleeding may occur without warning in the young as well as in the aged. One must not be misled, therefore, by the youth of a patient, for the subarachnoid bleeding may be entirely independent of any manifest evidences of injury. It is at once apparent that such a situation may give rise to a most perplexing medicolegal problem.

Subdural hematoma is a not uncommon complication in the course of head injuries. It consists of an encysted collection of blood between the dura and arachnoid membranes usually over the convexities of the cerebral hemispheres. These hematomas may develop as a result not only of severe trauma, but the injury sustained may be so slight, that the patient sometimes denies the occurrence of any trauma whatsoever. The interval between the accident and the fully developed systems of subdural hematoma may vary from a few hours to a few months and even years. This is due to the fact that the symptoms make their appearance very insidiously and on the other hand may do so very rapidly. The most usual picture of the fully developed subdural hematoma is headache, mental disturbances, vomiting, unequal pupils, pyramidal tract signs, and convulsions, either local or generalized. A most disconcerting phenomena, is the fact that lateralizing signs are not of great significance in cases of subdural hematoma, since the lesion is often found on the side opposite to that which is indicated by the symptoms.[16] It is thought that the ipsolateral hemiplegia is produced by the pressure exerted on the opposite hemisphere of the brain, the brain being pushed over by the soft subdural mass with a dislocation of the brain and the brain stem to the opposite side with an encroachment of the incisura of the tentorium on the contralateral crus as a result of downward pressures. Why this does not occur as a rule in brain tumors and occurs so frequently in subdural hematomas is still a disputable problem.

The question of disability is dependent upon the individual. There is no doubt that many, though afflicted with a post-traumatic neurosis, find it difficult to adjust themselves to the environment in which they fitted so well, prior to the injury sustained. Many of these people are, therefore, honestly and relatively, if not actually, totally disabled in spite of all so-called scientific tests. Others with severe head injuries often adjust themselves perfectly. It is almost superfluous to state that those with complete hemiplegias, aphasias, and those with mental changes of a psychotic nature fall into the category of those totally disabled. Permanent injuries such as those mentioned entitle one to the remuneration incident to permanent and total disability, and partial disability where there are signs of improvement in the injuries sustained. There is no doubt that malingering and dishonesty are the causes of many post-traumatic sequelae and ill-deserved compensations. There are many pitfalls for the unwary examiner but the clinically trained and

discerning eye can often detect the attempted simulations of the fraudulent pretenders.

## CONCLUSIONS

1. Head injuries give rise to immediate and remote symptoms and are important in so far as they effect the intracranial contents.

2. The acute manifestations of head injury are due to cerebral edema or intracranial hemorrhage.

3. Conservatism is the rule in management, with operative intervention properly performed when definitely indicated.

4. The remote symptoms are varied and more exhaustive encephalographic studies are advocated to assist both in the diagnosis of the conditions presented and their possible therapuetic effect.

5. The appraisal of the degree of disability requires the utilization of every clinical procedure available in addition to evidence of adequately sustained injury.

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# CASE REPORTS

## SUPPURATIVE BRONCHIECTASIS

### ITS SURGICAL TREATMENT

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WHEN Forestier, in 1922, first introduced lipiodol, a new advance in radiological diagnosis came into being. Particularly was this true in the study of pulmonary pathology. For instance, Hedblom quotes Hartung as stating that in a series of 72 cases of bronchiectasis, he was able to make the diagnosis on *x*-ray examination in only 20 cases and in 39 cases he could not recognize the lesion or its location. With the use of lipiodol, the bronchial tree becomes well delineated and the diagnosis of bronchiectasis, its location, degree, type and extent offers no great difficulty. In a series of routine bronchographic studies, it was very surprising to find how often bronchial dilation of moderate degree gave clinical symptoms suggestive of a very advanced process. On the other hand, we find pronounced dilatations of the bronchi giving meager clinical symptoms. It is the degree of infection in the bronchi and the surrounding lung parenchyma and not the extent of the bronchial dilatation which is largely responsible for the clinical picture of bronchiectasis.

In a series of cases studied by Trojanowsky, Fox and Chaplin, bronchiectasis was present in the left lung in 63 per cent; the right lung was affected in about 36 per cent.

The surgical aspects of unilateral suppurating cases only will be discussed here.

The pathological aspects of this disease in the light of recent investigations have developed our new conceptions of the disease to such an extent that it will be impossible to discuss them here. However, it is a well-established fact that anaerobic infection of the bronchial tree plays a leading role in the causation of this disease and its complications.

The complications of suppurative bronchiectasis make this disease a very serious problem. The three most important complications are empyema thoracis, brain abscess and amyloid disease. As a result of its slow development, the empyema is usually well walled off. It is not by any means a rare complication. In most instances local drainage will be sufficient. A chronic empyema with a complicating bronchial fistula should always arouse a suspicion of an underlying bronchiectasis or lung abscess. The response to simple drainage will largely determine what further treatment will be necessary, such as thoracoplasty or even lobectomy.

Brain abscess is the next most serious complication. Tuffier observed 6 brain abscesses in 45 cases. Lord, in observing a similar number of cases, found 3 brain abscesses and 7 cases of meningitis. Schorstein believes that brain abscess occurs in about 20 per cent of bronchiectasis cases. The relation of brain abscess to pulmonary suppuration has been observed for a long time. Even though the embolic theory may seem very attractive, yet it is difficult to explain why other organs in the body are not more affected, because the organisms must reach the aorta before reaching the

carotid vessels. It would be logical to assume that other organs in the body besides the brain would become involved almost as frequently. But such is not the case. Ballon, Singer and Graham in their discussion of bronchiectasis state: "Moreover, in general pyemia abscess of the brain is rare even when abscesses are present in the lung."

The treatment for this complication has had little success for the following reasons: its onset is often insidious; the diagnosis of single or multiple abscesses is difficult to make; and finally, localization often cannot be accurately made. Fortunately, this complication is more frequently single than multiple and involves the left more frequently than the right side of the brain. However, instances of recovery following surgical drainage have been reported by Roulland, Barling, Hurst and Gardner who have each reported one case.

Less dramatic in its onset and yet ultimately fatal is amyloid disease. This disease following pulmonary suppuration does not differ from that due to chronic suppuration in other parts of the body. It is a late complication. Its presence is suggested by the appearance of much albumin in the urine and enlargement of the liver. Its recognition is important since its presence is a contraindication to operation. Bennhold's congo red test is very helpful in recognizing this complication. There are other complications which, though serious, never approach in frequency those just mentioned. Fatal hemorrhage from ulceration of the bronchial wall has been reported by Sauerbruch, Küttner, Korte and Hedblom. Hemorrhage in bronchiectasis is more severe and more often fatal than in pulmonary tuberculosis. Thorp, in observing 53 cases in children, found 19 with a mild nephrosis and 5 with a severe hemorrhagic nephritis. Cardiac involvement and arthritis have also been observed in many cases.

Bronchiectasis becomes a chronic disease from the moment of its establishment. There is little evidence that spontaneous cures have ever occurred. It is conceded that not all cases of bronchiectasis will progress to the stage where radical treatment will be necessary. This discussion will consider only those cases of bronchiectasis which have failed to respond to non-operative measures and which are limited to one lobe.

The first radical surgical procedure practiced was incision into the lung and attempted drainage of the underlying infected area. Pathological studies soon showed the impossibility of adequately draining multiple bronchial cavities by a single incision. Clinically the method soon became obsolete. Newer experiences in the treatment of pulmonary tuberculosis suggested the use of compression therapy. Pneumothorax was first tried. The results were not lasting nor particularly good. Pneumothorax cannot compress the dilated bronchi. The amount of expectoration may be somewhat decreased but the underlying infection is still present. Pneumothorax may be of some benefit as a preliminary measure in lobectomy. Whittemore and Balboni, from their experience, state that in successful cases the pneumothorax must be kept up for a long time and this is often difficult of accomplishment. The results in a large series of cases have been disappointing. Graham, in 1921, and Zaaijer, in 1927, used compression therapy by means of tamponade. Sauerbruch also used tamponade. The reported results have been so meager that the method has found no extensive use as yet.

The author resected the sixth, seventh and eighth ribs in a girl twenty-four years of age for a moderate degree of bronchiectasis limited to the left lower lobe. The expectoration amounted to about 5 ounces of purulent foul-smelling sputum in twenty-four hours. But the patient came for relief for a persistent and vexing cough. Intrapleural tamponade was used against the left lower lobe and after three months, the sinus had closed. A subsequent bronchogram showed a very poor filling of the bronchial tree of the lobe and a very definite diminution in its area. Clinically the patient

when seen a year after her operation, no longer complained of cough, but raised about a teaspoonful of sputum in the morning. She was definitely improved.

Bronchoscopic treatment must be considered important in the removal of local causes, such as foreign bodies, dilating strictures and aspirating dilated bronchi to promote drainage. But it is doubtful whether bronchoscopic treatment alone can cure bronchiectasis. On the other hand this treatment can undoubtedly improve temporarily at least those patients who prefer less radical treatment. Clerf believes that bronchoscopic treatment will help a mild bronchiectasis due to a naso-pharyngeal infection.

Phrenic neurectomy has appealed to many because of its simplicity and for its effect on basal lesions. The results of this operation have been confusing. There hardly can be more than a slightly effective compression of the bronchi. Actually the elevation of the diaphragm causes the dilated bronchi to assume a more horizontal position and so promotes drainage. Improvement does undoubtedly occur in some cases but only for a short time. Too often this operation has given a false sense of security to both patient and surgeon. In the interim the process has insidiously spread, and a chance for a real cure has been lost. Oakley, for instance, reports 17 phrenic neurectomies with failure in 4 cases, relapses in 6 cases and complete relief in 7. Davies has performed 25 phrenic neurectomies with no improvement in 10; 5 patients were temporarily improved to become worse eighteen months later. One had complete relief for two years to be followed by hemoptysis and death. Nine were apparently improved.

The author has not used this operation because it was felt that the results did not justify its use except as a preliminary to lobectomy.

More encouraging than phrenic neurectomy has been the use of thoracoplasty. Hedblom has been the most enthusiastic advocate of this procedure. This operation implies a complete collapse of the chest wall by extensive resection in several stages of the upper eleven ribs; for the complete collapse of the base, a complete resection of the whole length of the lower ribs is necessary. In his most recent report Hedblom states as follows:

> In 1926, I reported 14 cases in which I had done a thoracoplasty in five stages without operative mortality. Three of the patients are entirely relieved and have remained symptom-free since. Seven of the patients have continued to raise sputum amounting to 10–20 per cent of what had been raised before the operation. Six of the seven have been working regularly. Four whose symptoms were greatly relieved, died from ten months to two years after operation.

Then Hedblom reported 18 additional cases. Four of these patients died, the remaining 14 were more or less improved. Two died later. In all, 32 patients were operated on, 21 are living. A review of the literature does not seem to reveal results from thoracoplasty which are particularly striking as shown by the published reports of Harrington, Sauerbruch, Brauer and recently by Janes.

The author has twice performed this operation. One patient died eight weeks after the second stage of the thoracoplasty due to a septic pneumonia developing in the other lung; the sputum had decreased to about 30 per cent of the original amount. The other patient was two months pregnant at the time of operation and raising over 16 ounces of foul purulent sputum in twenty-four hours. She was delivered in due time without any serious difficulty. When seen six months after delivery the patient showed slight general improvement and her sputum had decreased to about 7 ounces in twenty-four hours. Thoracoplasty should be considered in bronchiectatic cases rather in the light of a preliminary than as the main surgical procedure, because lobectomy can then be performed secondarily and probably with less risk. In cases in which the extent of the disease contraindicates removal of lung tissue

thoracoplasty may then be indicated in multiple stages.

We leave for final consideration extirpation of the lobe. When this is possible, we believe this procedure to be the best. In 1923 Graham introduced his operation of cautery pneumectomy. This was an important contribution. This procedure is an advance over that of Garré, Sauerbruch, Körte and others who at the time performed a type of pneumonotomy. Their good results were in abscess of the lung. Graham's operation is more extensive and aims not to remove the whole lobe but only its diseased portion. According to Graham "bronchiectasis associated with multiple lung abscesses and chronic lung abscesses with secondary bronchiectasis are the types most suited for cautery pneumectomy."

Graham, prior to 1930, performed 54 cautery pneumectomies (not including carcinoma of the lung). Sixty-six per cent were definitely improved. The immediate mortality was 11 per cent, the late deaths 22 per cent. Bronchial fistulae were present in 33 per cent of the surviving patients. The chief objections to the operation appear to be:

(1) Prolonged convalescence.
(2) Bronchial fistulae.
(3) Postoperative hemorrhage.
(4) Possible injury to underlying structures by the cautery.
(5) Air embolism.
(6) Empyema.

This operation should be the procedure of choice in cases which are septic with marked leucocytosis and high fever. The report of the following case illustrates the value of cautery pneumectomy in certain phases of bronchiectasis:

Case 1. A. H. a boy aged twelve years. Admitted to the Broad Street Hospital Nov. 23, 1931.

*History:* Five years ago the patient developed pneumonia which became complicated by an empyema on the right side. The patient was operated upon at another hospital twice with rib resection and was finally discharged as cured. Three years later the patient began to cough and raise large amounts of sputum, especially in the morning. During this time he felt feverish and chilly and was rapidly losing weight.

*Examination:* The patient was emaciated, appeared chronically ill and his face was flushed. He was slightly cyanotic and his fingers and toes were markedly clubbed. The breath was foul and the patient expectorated about 16 ounces of foul sputum in twenty-four hours. On the right side of the chest was a healed scar following the empyema operations. There was increased dullness over the lower half of the right chest posteriorly with areas of bronchial breathing with many moist rales. Neither the spleen nor the liver was felt. The urine contained no albumin. *X*-ray examination showed the heart slightly displaced to the right side and an atelectatic right lower lobe could be made out through the heart's shadow. Examination with lipiodol demonstrated a severe bronchiectasis of the cylindrical type limited to the right lower lobe.

*Operation:* November 27, 1931. Under gas oxygen anesthesia, the author resected the seventh, eighth and ninth ribs from the angle to the posterior axillary line together with the intercostal bundles and periosteum, exposing a window of parietal pleura. The pleura was painted with tincture of iodine and the wound closed, leaving a layer of iodoform gauze between the pleura and the skin. The wound was reopened fifteen days later. After first coagulating the exposed pleura and underlying adherent lung with a disk electrode, the lung tissue was then scooped out using the high frequency current throughout. The hemorrhage was slight. The wound was again packed with iodoform gauze, but the skin was not closed. Two subsequent cauterizations were performed at weekly intervals using the actual cautery to destroy the remaining infected tissue. The patient was discharged nine weeks after admission with a single bronchial fistula. He has since gained 27 pounds, has had no fever and only an occasional cough. His expectoration rarely exceeds 1½ ounces in twenty-four hours and the foul odor of the breath has disappeared. The bronchial fistula discharges a moderate amount of purulent material which is not foul. No attempt will be made to close the fistula yet.

With improvement in surgical technique and better localization of the disease by

the use of lipiodol, lobectomy in recent years has again been advocated. Up to 1914, 16 lobectomies with 8 deaths had been reported. In a personal communication to Graham, Lilienthal states that he has performed 42 lobectomies. This group of resections includes some subtotal pneumectomies and cases in which resection of a greater part of a lobe was performed. The mortality was 64 per cent. This is the largest series of lobectomies reported by an individual surgeon. In 1927, Sauerbruch reported 23 lobectomies for lower lobe bronchiectasis with 3 deaths. Nissen, in 1931, reported 38 lobectomies from the Sauerbruch clinic with a mortality of 10 per cent, a most enviable record. Whittemore, by his exteriorization method, has had 10 cases with a 30 per cent mortality. Brunn reports 2 deaths in 9 cases. Shenstone and Janes report 17 cases, 16 of these were done in one stage. Six cases were cured, 3 improved, 2 unimproved and 5 died. Alexander has recently reported 18 cases with 3 deaths. Roberts and Nelson reported 10 cases with 2 deaths, 6 patients symptom-free and 2 back at work with slight symptoms. The cases in which the author has performed lobectomies have been treated by the usual conservative methods and were finally referred for lobectomy because of the hopeless condition of the patient. Lobectomy is obviously the ideal treatment for a chronic disease limited to one of the lobes of the lung. Ballon, Singer and Graham have found reports of 212 lobectomies to date.

Before accepting a patient for lobectomy, an exact localization of the disease with lipiodol is made. Amyloid disease and an impaired cardiovascular system contraindicate lobectomy. Due to the large amount of sputum, there is considerable danger of bronchopneumonia. Bronchoscopic aspiration twice weekly with daily correct postural drainage will lessen this danger considerably. Bronchoscopic aspiration immediately before operation should be performed. Temporary phrenic paralysis has not been used in any of the following cases. However, this procedure has undoubted advantages when making a dissection of the lobe from the diaphragm. Preliminary pneumothorax is not of any real value, because it is often impossible to induce an efficient pneumothorax due to adhesions.

The operative procedures will not be taken up separately but will appear in the reports of the following cases in which lobectomy has been performed:

Case II. W. S., male, aged twenty-one years, was admitted to the Broad Street Hospital April 30, 1932.

*History:* For the past two years, the patient has noticed that he was short of breath and raised large amounts of thick foul sputum. The sputum has never been bloody. There is no history of any acute respiratory infections or any operations.

*Examination:* The patient appeared chronically ill and cyanotic. Over the lower half of the left chest posteriorly there was impaired resonance with areas of bronchial breathing with many moist rales. Bronchography revealed a marked bronchiectasis of the left lower lobe of the cylindrical variety.

*Operation:* (May 3, 1932.) The author resected the seventh, eighth and ninth ribs from the angle to the posterior axillary line together with the periosteum and intercostal bundles leaving a window of parietal pleura. The pleura was then incised and the lobe freed from its attachments in the chest except at the hilus which was well defined. The pulmonary artery to this lobe was isolated at the hilus and ligated. The lobe was then isolated by completely surrounding it with iodoform gauze and the chest closed.

A stab wound was made below the incision for internal drainage. After ten days the wound was re-opened and the lobe amputated at the hilus. The hilus was then doubly transfixed and sutured to the under surface of the lobe above. The wound was closed except at the lower angle which was left open for drainage. Convalescence was smooth until seventeen days later when a laparotomy was performed for an obstruction due to a herniation of the jejunum into the superior duodenal fossa. He was discharged four weeks after the first operation with a bronchial fistula. He was greatly improved. The bronchial fistula was healed

within the next three weeks. The chest wound healed about three months later. He gained 25 pounds and the sputum had almost disappeared. He still coughs occasionally.

Case III. R. S., male, aged twenty-seven years. Admitted to the Broad Street Hospital September 8, 1932.

*History:* As a child he had severe attacks of "bronchitis" which came on quite frequently. He always had a severe cough, raising large amounts of thick foul sputum. Hemoptysis was noted once six years ago.

*Examination:* The patient appeared chronically ill and flushed. Over the posterior aspect of the left chest the breath sounds were harsh and areas of bronchial breathing with many moist rales were heard. Bronchography showed a marked bronchiectasis of the saccular type involving the left lower lobe.

*Operation:* (September 10, 1932.) The author resected the sixth rib from the angle to the posterior axillary line. The pleura was then incised and a rib spreader inserted, exposing the lower lobe. The artery to the lobe was not ligated. The lobe was freed from its attachments and the hilus clearly defined. The lobe was then isolated, using rubber dam and the chest wound closed, with closed drainage. Ten days later the chest was re-opened and the lobe amputated at the hilus. A plastic exudate had formed isolating the lower lobe from the rest of the pleural cavity. The stump was doubly transfixed and sutured to the under surface of the upper lobe. The chest wound was then closed except for the angle at the lower end of the wound. This opening served as an open drainage site which could also be used for packing gauze into the pleural cavity in case of hemorrhage from the hilus stump. This patient was discharged twenty-seven days after the first operation in good condition. The bronchial fistula closed in five weeks and the chest wound healed seven weeks later. The patient gained over 20 pounds, coughs rarely and at most raises about 1½ ounces of sputum in twenty-four hours.

Case IV. M. T., female, aged twenty-one years, clerk. Admitted to the New York Post Graduate Hospital July 29, 1933.

*History:* Without any previous pulmonary history, the patient began to have attacks of coughing five years ago immediately following a pulmonary hemorrhage. At irregular intervals since she has had hemoptysis. All examinations for tuberculosis were negative. She coughs up about a "cupful" in twenty-four hours. Bronchoscopic drainage at intervals has afforded her some relief.

*Examination:* The lungs showed poor expansion. At the right base there was impaired resonance and in this area patches of harsh breathing and many moist rales could be heard. Bronchography showed a cylindrical bronchiectasis of the right lower lobe.

*Operation:* (August 3, 1933.) The same procedure was followed as in the preceding case. The patient was discharged twenty-five days after the first operation, expectorating about 2 ounces in twenty-four hours. She felt much improved. The bronchial fistula healed in six weeks and the chest wound closed two weeks later. About three months after leaving the hospital, the chest was aspirated and a small amount of bloody serum was obtained. This serum was apparently obtained from a pocket visible on *x*-ray examination. This pocket has since disappeared and has apparently been filled in by the expansion of the remaining lung tissue. The patient is now in excellent health.

Case V. M. Ty., aged twenty-seven, housewife. Admitted to the New York Post-Graduate Hospital October 19, 1933.

*History:* The patient has had "bronchitis" since childhood. About three weeks ago the patient was compelled to go to bed because of severe pain in the left chest which was diagnosed at the time as pleurisy. She had chills and fever and perspired freely. She coughed frequently and raised variable amounts of foul sputum. The patient was finally compelled to enter the hospital for relief.

*Examination:* The patient appeared chronically ill and seemed to have lost considerable weight. Her face was flushed. Fingers and toes were clubbed. Heart was normal. Respiratory movements of the left chest were shallow. There was impaired resonance over the left base posteriorly with diminished breath sounds and patches of bronchial breathing throughout. Fine moist rales were heard over both bases posteriorly. On *x*-ray examination the mediastinum was displaced to the left. A bronchogram revealed a pronounced cylindrical bronchiectasis of the left lower lobe.

*Operation:* (November 9, 1933.) The technique followed was the same as described in the preceding lobectomies. At operation it was noticed that the upper lobe was sufficiently

adherent to the chest that when the pressure of the gas oxygen anesthesia was reduced to atmospheric pressure, the upper lung did not collapse. This observation is made at each first stage lobectomy to determine the sufficiency of the attachment of the upper lung to the chest wall. A rather unusual complication followed the lobectomy in that the upper lobe became atelectatic probably due to a bronchial obstruction. This caused the upper lobe to pull away from the chest wall in its entirety and shrivel up to the size of a fist. A total empyema followed. At this time, the patient was in no condition to stand further operative interference. It was hoped, however, that her condition would improve sufficiently at a later time to allow the performance of a thoracoplasty. Under irrigations of the empyema cavity, the condition of the patient improved to such an extent that she was permitted to go home five weeks after the first operation. Three weeks after leaving the hospital the patient died suddenly from what her family physician believed to be an embolism.

The pathological features of all these cases was very impressive. The lobes in all cases were markedly adherent to surrounding structures in the chest. The color was no longer that salmon pink shade found in the normal lobe in vivo. Instead, we see a purplish blue to dark slate color. There was considerable induration throughout the lobe with very little crepitation noticeable. On section they all showed markedly dilated and thick-walled bronchi. The tissue around the bronchi appeared hepatized, hemorrhagic and in some cases undergoing suppuration.

## CONCLUSIONS

1. Suppurative bronchiectasis is a serious disease.

2. Its early diagnosis and accurate localization offers no great difficulty.

3. The type of operation will depend somewhat on the physical condition of the patient and the extent of the disease.

4. Although this series is too small to justify any conclusions on a percentage basis, it seems that lobectomy along the lines of the technique above described can be recommended to offer the best possibilities for an effective result in unilateral suppurative bronchiectasis.

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# PRIMARY CARCINOMA OF THE URETER

## WITH REPORT OF TWO CASES*

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PROGRESS in knowledge of a subject is made chiefly by intensive study devoted to it over a certain period of time. Every now and again we see this rule, which is self evident in the laboratory, applied also in the literature of medicine. Sometimes this intense interest in a subject is limited to the literature of one country, at other times the interest tends to be world-wide. By this spontaneous and unpremeditated cooperation of researchers or clinical observers or both, an obscure subject will be placed for a period in the front of the stage and direct and oblique lights trained upon it, with the result that we learn in a comparatively brief time all that it is possible for the moment to learn about it. At such a time it is peculiarly the duty of everyone who can contribute an observation in point, whether it offers any unusual features or is wholly typical, to add it to the general stock, so that it may extend or solidify by confirmation the knowledge that we already possess on the matter.

Something like this has been occurring throughout the world, but more especially in this country and in Germany, of recent years with respect to primary carcinoma of the ureter. The first description of a case appeared in 1841. The first report in the English language was in 1884. In 1924 Kretschmer[1] collected and published 35 cases. This appears to have been the first collection of cases of primary carcinoma of the ureter. Two years later Blatt,[2] in Vienna, made a collection of 40 cases. Rousselot and Lamon[3] went over the literature again in 1930 and published the main data on 50 cases. The following year Renner[4] presented a closer analysis of this collection from certain points of view, eliminating 3 cases and adding one case that was missed, and reported an exceptional case of primary carcinosarcoma of the ureter. To the total of 48 cases of primary carcinoma of the ureter as collected by Rousselot and Lamon and amended by Renner, there can be added about a score of cases published since 1929 or too late in that year to be included by Rousselot and Lamon. With the two that I am reporting the number is thus brought up to around 70.

This rapid increase in reported cases is due not alone to the stimulation of interest by the afore-mentioned collections and discussions but also to advances in methods of urologic examination. It is noteworthy that it is chiefly in the last three years, since Rousselot and Lamon's[3] comprehensive study was made, that we are getting reports of cases diagnosed before operation or autopsy frequently enough to be regarded as anything more than striking exceptions exemplifying, perhaps, a clever guess rather than a diagnosis. This fact is encouraging as indicating the real advance that technical measures together with closer observation of a greater number of cases is already bringing. Carcinoma of the ureter grows rather slowly and does not, as a rule, metastasize early. At present the prognosis is bad, but with early diagnosis and early operation, it should be fairly good. In Rousselot and Lamon's[3] collection of 49 cases, 30 of the patients died under treatment or shortly after leaving hospital. The only five-year cure in the literature appears to be that in

* Read before the North Carolina Urological Association, Pinehurst, N. C.

Crance and Knickerbocker's[5] case. As in all cases of carcinoma, the emphasis must be placed on early diagnosis, and for this, all the resources of modern urologic examination must be employed.

The concealed location of the ureter makes a definite diagnosis impossible without technical aids. The symptom picture is not characteristic. Of the classical triad: hematuria, pain, tumor—there is not one that can be depended upon always to be present, and any one or all of them together, when present, may equally well mean other conditions than ureteral cancer. It must, however, be emphasized that the technical methods also: cystoscopy, ureteral catheterization and pyelography —can easily leave one in the lurch. It is viewing the composite picture of symptoms and of special signs observed on urologic examination that one is able, in certain cases offering favorable conditions, to determine the nature of the condition with some degree of certainty before opening the body.

Hematuria has been reckoned to be present in from 50 to 75 per cent of cases. It is the typical bleeding from a malignant tumor, spontaneous, capricious, appearing and disappearing suddenly. It may be of any degree from massive, producing a dangerous anemia, to so slight as barely to tint the urine. It may be microscopic. It is frequently intermittent. A history comparatively often encountered is that there was a sudden hematuria, lasting a short time, possibly recurring once or twice, but leaving an interval of months, sometimes a year or two (in von Sauer's[6] second case three years) between the last occurrence and the symptoms, which may or may not include bloody urine, which finally bring the patient to urologic examination.

A similar history of one or more attacks of pain occurring at some time in the past and not repeated is met with in a number of cases. These attacks are likely to have been of colicky nature. Grüneberg[7] suggests that they may be caused by spasm of the ureter with stasis and may point to the very beginning of the disease. In the case that he describes pain was limited to two attacks seven months before the diagnosis, and the diagnosis was made at an unusually early stage, before secondary injury to the kidney had taken place. Kneise[8] also reports a case diagnosed when there was as yet only slight enlargement of the corresponding kidney, in which there had been two colics one year and five months previously, with blood-stained urine. Kneise describes two kinds of pain as found with ureteral tumor, a renal pain caused by the stretching of the kidney pelvis by the damming back of fluid because of the ureteral obstruction, and sciatica from pressure on the sacral plexus. In the latter case the condition is already far advanced and prognosis is bad. In Ockerblad and Helwig's[9] case pain was a late symptom and these authors consider that the greater part of the pain was due to the extension of the inflammatory zone of the growth so that the mass involved not only the adjacent viscera but also the great vessels and nerves; pain and swelling of the leg on the affected side were marked. Stewart[10] has named three types of pain and assigned their causes: colicky, caused by passage of coagula; more constant, caused by dilatation of the renal pelvis; severe or lancinating, caused by the infiltrating malignant tumor itself. Chauvin and Cerati[11] speak of heavy, constant lumbar pain. The location of the pain has been described as the lumbar region, the renal region, the back and the abdomen. It may radiate from the kidney to the bladder. It has been referred to the hip in a number of cases.

It is seldom that a tumor of the ureter is itself palpable. It may sometimes be palpated from the vagina in a woman or from the rectum in a man, but even if a tumor is felt the ureter will be only one of its possible sites. It may be a glandular metastasis or an intestinal tumor. In the case of a woman, tumor of the adnexa will be the more likely diagnosis. The tumor or

enlargement that is palpated externally is almost always a hydronephrosis or hydroureter (or hematonephrosis or hematoureter). It is therefore a late symptom, since it takes time, first for the carcinoma to develop sufficiently to obstruct the ureter enough to dam back the urine, and secondly for the hydronephrosis or hydroureter to attain a size that would be palpable. The earliest symptoms observed may be those of infection of the hydronephrosis. Such was the fact in the case reported by Ockerblad and Helwig,[9] in which the only findings worthy of note when the patient was first examined were pus in the urine and fever. Von Sauer[6] points out the interesting fact that the degree of stasis and of distention does not necessarily run parallel with the encroachment of the tumor on the lumen of the ureter, since nervous influences play a part in the dilatation by relaxing the ureteral wall. The factor of interference with innervation is particularly important in the case of infiltrative growths.

Urgency, frequency, dysuria, nocturia and incontinence may be present, but are by no means constant symptoms. Complete anuria with coma has been noted on very few occasions. Sommer[12] reports such a case, with a primary tumor obstructing one ureter and a metastasis obstructing the other; and Klages[13] reports another, in which partial autopsy only was allowed, so that the cause of the anuria could not be definitely determined. The lumen of the left ureter was closed by tumor masses. He remarks that dynamic insufficiency of the kidney of the other side must be thought of in such a case, as well as the possibility of mechanical obstruction. A tumor of the urinary tract on one side of the body can act by nervous reflex to prevent secretion of urine on the other side. This is occasionally seen in sarcoma of the kidney in children. Glas[14] also saw a case of primary ureteral tumor with anuria, and Klages mentions that two instances of anuria with metastatic carcinoma of one ureter are to be found in the literature.

Cystoscopy may clear up the diagnosis at once by revealing a tumor protruding from the orifice of one of the ureters and permitting biopsy. Puffing of the mucous membrane around a ureteral orifice from edema is a suspicious finding. On the other hand, the cystoscopic findings may be normal. If hematuria is present and the bleeding is going on at the time of the cystoscopic examination, much information may be obtained, unless, of course, hemorrhage is so profuse as to obscure the picture altogether. In the first place, the question is settled as to the side affected. Then, much may be learned by close observation of the manner in which the blood is escaping. Grüneberg[7] gives as characteristic of ureteral affection the oozing of blood independently of ureteral peristalsis. In his case he was able to note the excretion of dye with the peristaltic wave while the blood dripped continuously, without relation to peristalsis. It is possible to obtain this sign only, of course, when the renal parenchyma is not too badly damaged to excrete the dye. In Grüneberg's case there was as yet no dilatation of the renal pelvis. Helfer[15] points out that if hydronephrosis is present, which will most often be the case when examination is made in a case of tumor of the ureter, the normal peristaltic rhythm is hardly to be expected. He observed, however, a movement of the ureter from time to time without escape of urine but with oozing of a few drops of blood from the orifice, which clung to its edges and clotted rapidly, not mixing with the bladder urine. This slight bleeding following peristaltic contractions he explains as caused by compression injury to a tumor situated in the lower part of the ureter. On this sign he correctly diagnosed a carcinoma in this situation which did not protrude into the bladder.

Another useful diagnostic observation in cases in which the cystoscopic examination is made in a period free from hematuria is the provocation of bleeding

by manipulation of a catheter introduced into the ureter until stopped by the tumor. This sign may be expanded by pushing the catheter up past the obstruction into the kidney pelvis, if this is possible. If the urine now withdrawn through the catheter is free of blood, while urine from just above and just below the obstruction is bloody, it has been definitely ascertained that the source of the bleeding is not in the kidney, and if it is in a normally formed urinary tract it must be in the ureter. But we still have to decide whether the obstruction is a tumor, a stone, or a traumatic or tuberculous stricture. There is the further possibility that there is no lesion but an anomaly of formation, the obstruction encountered may be the forking of a ureter fissure and the blood which is missed when we push the ureter higher up but is found again when we lower it to the level of the obstacle may be coming from a second renal pelvis. Extraureteral pathologic processes, such as enlarged retroperitoneal glands, which compress and kink the ureter, can also cause confusion by producing obstruction and bleeding on manipulation with the catheter. The catching of the catheter in a fold of mucous membrane can have the same result. Sometimes bits of tumor tissue will cling to a catheter that has been twisted about on the surface of a protruding tumor and allow of microscopic diagnosis without further effort. As a help in the differentiation from stone, Einar and Åkerlund[16] suggest the use of a waxed catheter, with subsequent examination of the waxed surface for scratches such as a stone would make. If after the catheter has been pushed past the obstacle into the kidney pelvis a hematonephrosis is evacuated through the catheter, there is strong reason, according to Einer and Åkerlund, for suspecting that the primary tumor is in the kidney pelvis and that the obstacle encountered in the ureter is an implant.

It is the *x*-ray examination to which we must look to bring a higher degree of certainty into the diagnosis after cystoscopy and ureteral catheterization have done their part in localizing the source of bleeding. The plain roentgenogram may rule out stone with considerable probability, but the pyelogram and ureterogram with contrast substance are necessary to rule out other causes of confusion and to show the exact location and the size of the tumor and the conditions in the ureter and in the kidney above which have arisen as its sequelae. Difficulty may be encountered in getting the contrast substance up past the obstruction. The intravenous method should be a great aid if the kidney retains sufficient function. All degrees of function and loss of function are encountered in the kidney above a ureteral carcinoma, depending, aside from infection, on the urinary stasis, which, in turn, depends on the size of the tumor and its site and the length of time it has obstructed the ureter.

There are two main types of filling defect, a brush-like shadow, produced by penetration of the contrast fluid into the folds and interstices of a papillary tumor, and a dish-like or helmet-shaped defect, when the structure of the tumor is solid. A tumor projecting into the lumen will be seen most clearly when it proceeds from the lateral wall, since it will not be covered by contrast substance. A lateral view will show up best a tumor proceeding from the anterior or posterior wall. If the growth is infiltrative one does not get such a filling defect but indistinctness of contour of the ureteral wall on the affected side, which has been compared to the effect of chiseling. If, as in one of my cases, the cancer does not project into the lumen but, spreading in the wall, compresses it on all sides, only a thread of contrast fluid will be present to cast a shadow in this portion of the ureter, or the ureteral shadow will appear entirely broken off at this level.

Einar and Åkerlund[16] refer to the similarity in the roentgen picture of ureteral tumor to the deformation of the

shadow seen in the case of tumor of the tubular parts of the digestive tract: the esophagus and the intestine. They state that if one obtains a dish-like spreading-out of the ureteral shadow just below a filling defect and one can rule out stone, one may diagnose ureteral tumor. The idea here appears to be that the tumor distends the lumen where it protrudes into it, but while the tumor appears as defect, the lumen leading up to it and widening as the tumor is approached, appears as shadow. Grüneberg[7] refers to a club-like widening of the shadow proximal to the filling defect. It should, however, be admitted that, as Davis and Sachs[17] point out, the visible filling defect in the roentgenogram is rarely in actual experience sufficiently clear-cut and definite to assure the diagnosis; the picture is likely to show evidence merely of ureteral block, such as might be caused by obstruction due to kink or stricture.

The greater number of primary carcinomas of the ureter reported have been papillary: 19 in the 48 cases collected by Rousselot and Lamon[3] and amended by Renner.[4] Grüneberg[7] found 14 cases of carcinoma simplex. Squamous cell carcinoma appears to be somewhat less frequent than carcinoma simplex. Rousselot and Lamon's collection contained only one case of adenocarcinoma. Kneise[8] and Cross[18] have since published 2 cases. It appears, therefore, that my case of adenocarcinoma belongs to the rarer findings in this generally rare location of carcinoma.

Statements differ as to the readiness with which carcinoma of the ureter metastasizes, but the general impression received from a study of the literature, in which one is impressed by the length of time elapsing between the earliest symptoms referable to the condition and the diagnosis and the fact that the patients were in so large a number of cases in good general health at the time of the diagnosis, is that metastasis to vital organs must be a generally late occurrence. The tumor may involve vital organs by local extension. In Navratil's[19] case, in which the first symptoms were one year and three months back, and in which there was peripheral paralysis of the lower extremity on the side of the tumor, the tumor tissue had grown without sharp demarcations into the cellular tissue of the corresponding side of the pelvis and into the bony substance of the sacrum and ilium and ensheathed the sacral plexus. In Ockerblad and Helwig's[9] case the tumor mass involved the viscera and filled half the abdominal cavity and had eroded the wall of the duodenum as far as the mucosa but had not penetrated the lumen. In one of my cases the appendix was found buried in the tumor mass, but its walls were intact.

Case 1. J. D., male, aged fifty-eight. Referred February 23, 1932, by Dr. Charles McGavran and Dr. Ed. Miller. Patient was well until six months before he came under observation, when he developed a pain in the region of the right kidney, referred to the groin, aching in character, progressive and associated with slight frequency and dysuria. There was no history of hematuria, no appreciable loss in weight. The pain in the right kidney was constant and very severe at times, requiring morphine frequently.

The patient had typhoid at nineteen years of age, influenza in 1918, no previous surgical operations. There was no history of cancer in the family.

General physical examination was negative. Rectal examination showed no prostatic enlargement.

*Examination of the urine* revealed 10 mg. of albumin, no sugar, many pus cells and several red blood cells per high field.

*Blood pressure:* 125/80.

*Blood:* Blood urea nitrogen: 20 mg. per 100 c.c. of blood. Red blood cells: 5,300,000. Hemoglobin: 95 per cent. Leucocytes: 10,000. Polymorphonuclears: 82 per cent. Blood sedimentation test: One-half hour 40; one hour 30; one and one-half hours 30.

*Two-hour renal function test:* First hour 70 per cent; second hour 10 per cent; total 80 per cent.

*Cystoscopic examination* of the bladder revealed nothing of significance except an acute

congestion of the vesical mucosa about the right ureteral orifice. Because of its appearance, a specimen was removed by means of the cystoscopic rongeur for study. Microscopically nothing was found but large clumps of polynuclear leucocytes and inflammatory exudate. Diagnosis: sub-acute inflammation.

Ureteral catheters No. 6 F. passed without difficulty to the left kidney, but on the right side the catheter would not pass for more than 2 cm. before obstruction was encountered.

The function of the left kidney was normal as to appearance time and concentration of

Fig. 1. Case 1. Inability to pass catheter up right ureter.

Fig. 2. Case 1. Three-inch elongated constriction of distal end of right ureter with hydroureter and hydronephrosis above stricture.

Fig. 3. Picture of Figure 2, retouched to emphasize contrast.

Fig. 4. Case 1. Diagrammatic drawing to show extent and location of tumor.

the dye. There was no function of the right kidney in thirty minutes.

*Right Pyelogram:* The kidney pelvis and calices were widely dilated but incompletely filled because of an insufficient amount of sodium iodide solution. The ureter was very large and dilated down to the brim of the true pelvis, where a sharp and elongated constriction developed as if something involved the wall of the ureter from the above point down to the bladder, a distance of fully 3 inches.

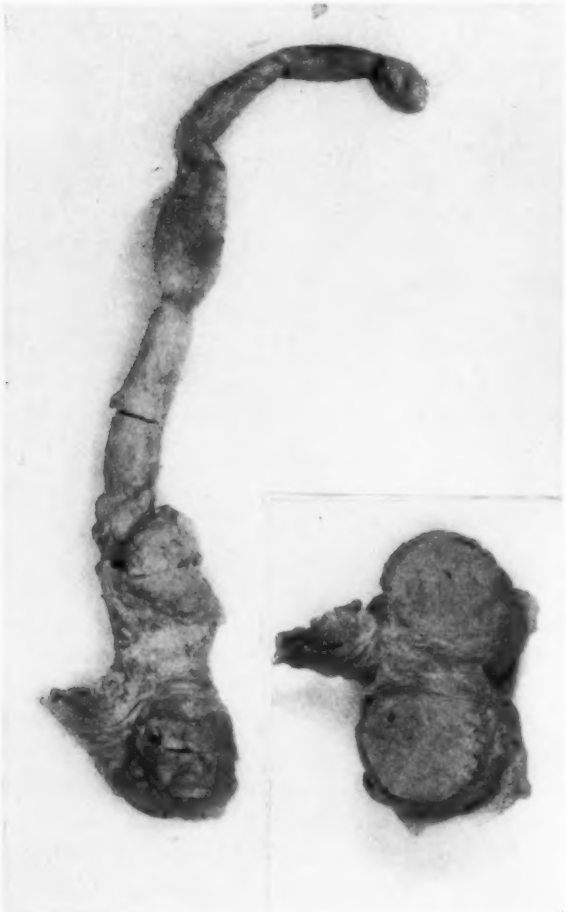

Fig. 5. Case 1. Actual photograph of specimen showing ureter which is greatly enlarged, thickened, infiltrated and replaced in its distal portions by a solid tumor. In its proximal portions ureter is widely dilated. Insert reveals cross section of tumor mass practically obliterating lumen of ureter.

*Impression:* 1. A functionless right kidney, hydronephrosis and megalo-ureter.

2. Elongated impassible stricture of right ureter involving the lower 3 inches, probably due to new growth from its very appearance.

*Suggestion:* Nephrectomy and ureterectomy if possible.

*Operation:* Under gas-ether anesthesia, the right kidney and ureter were exposed. Fully one-half pint of fluid was found in the pelvis and calices. The ureter was 6 to 8 times larger than normal and very tortuous throughout. There were many adhesions. A large mass could be felt at the brim of the true pelvis, which involved the surrounding tissue. The kidney and upper ureter were removed. It was impossible to remove the lower third of the ureter. The postoperative convalescence was satisfactory.

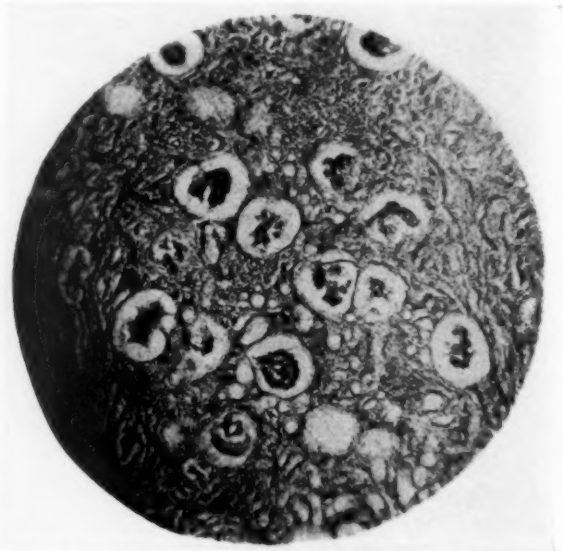

Fig. 6. Photomicrograph. A diffuse densely cellular tumor with alveolar changes. No papillary structures present. Some pathologists state this is a malignant transformation of a papillary carcinoma into a massive infiltrating alveolar type of adenocarcinoma.

*Pathologic Report of Kidney:* The outer surface showed numerous ecchymotic hemorrhages. The pelvis and calices were typical of hydronephrosis.

*Subsequent Course:* The patient was discharged from the hospital. Two months later pain developed in the right lower quadrant and became more severe than it had been at any time before. Swelling appeared in the right leg. Five months after operation I cystoscoped the patient at his home and found a tumor extending from the right ureter, the size of the end of one's thumb. The bladder itself was not involved except at the ureteral orifice, where there was much acute inflammatory change. Six months after operation the patient died.

*Autopsy:* A carcinomatous-like mass was found to involve the lower 3 or 4 inches of the right ureter, the posterior surface of the bladder

where the ureter entered the bladder and the iliac vessels on the right side. The appendix and cecum were involved in this mass and it was quite evident that it took origin in the right ureter near the bladder.

On *macroscopic examination* the ureteral

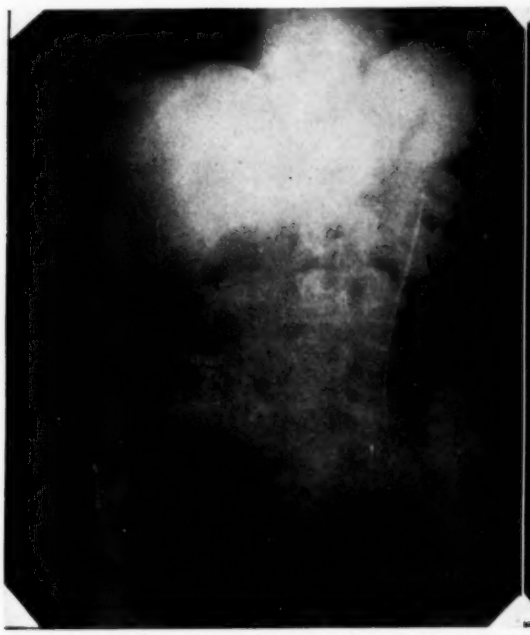

Fig. 7. Case 11. Inability to pass catheter beyond middle third of right ureter.

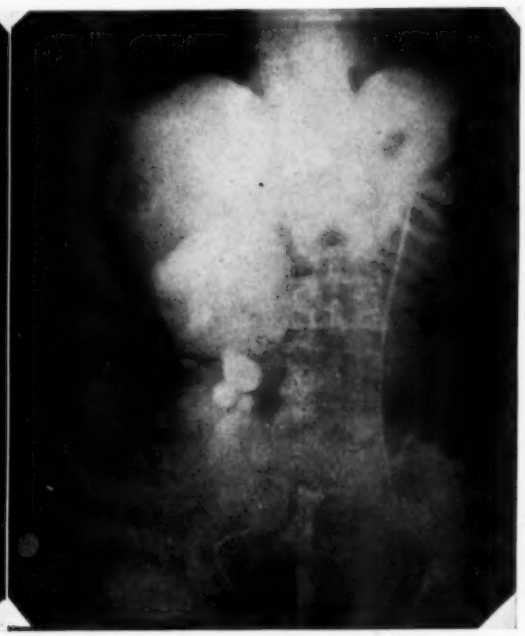

Fig. 8. Case 11. Right pyelogram and ureterogram showing complete obliteration of all normal markings of kidney and ureter. Hydronephrosis. Filling defect of lower ureter at site of tumor.

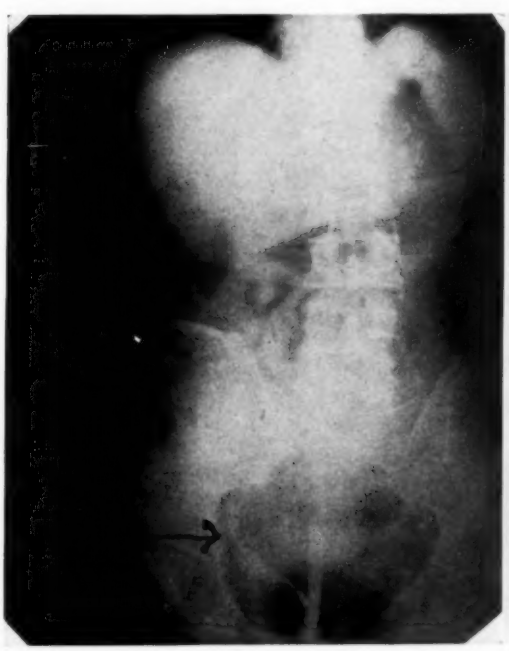

Fig. 9. Case 11. Ureterogram of ureteral stump, also showing filling defect.

Fig. 10. Case 11. Diagrammatic drawing to show location of ureteral tumor and outline of kidney and ureter.

pulled down behind the bladder. Fully three-fourths of the appendix was buried in the new growth. From the appearance of the growth wall above the site of the growth is of paper thinness, elastic and distended by a large amount of thick, purulent appearing substance.

On sectioning at the site of enlargement, the cut surface is firm, solid and grayish-white. The ureteral wall is here greatly thickened and

Fig. 11. Case II. Photograph of specimen; ureteral stump opened, showing papillary tumor attached to wall.

the lumen obliterated. The appendix is incorporated in the growth, but the growth appears to be entirely without the wall of the appendix.

*Microscopically*, the sections through the tumor are densely cellular, so that all characteristics of ureteral structures are obliterated. The epithelial cells vary considerably in size and shape. Many mitotic figures are noted. Papillary arrangement is not present. The entire growth is adenomatous in character.

*Pathologic Diagnosis:* Adenocarcinoma of the ureter with metastatic changes in the appendix and mesentery.

*Comment:* 1. There was no history of gross hematuria, although microscopic blood was found in the urine. There was

Fig. 12. Case II. Photomicrograph revealing papillary overgrowth of epithelial cells of mucosa, producing long, papillary masses. Epithelial cells show malignant anaplasia, irregularly arranged and diffuse in some areas. Papillary carcinoma of ureter.

no loss in weight.

2. Note the very interesting ureterogram.

3. Pain was confined to the right kidney region, referred to the groin, until the terminal stages, which were associated with great pain and swelling of the right leg and thigh.

4. There was no evidence of malignancy in the kidney or bladder.

5. The parts involved showed destructive changes.

Case II. C. E., male, aged seventy-six. Referred May 12, 1932, by Dr. J. J. Coons. The patient was well for his age until one year previously, at which time blood appeared in the urine, but cleared up in a few days. He had no more hematuria for four months, when it again appeared, but this, too, subsided in a few days. There were several subsequent attacks, with clots appearing at times. A few days prior to consultation, there was profuse hematuria with many clots. He complained of no pain, but slight discomfort in the right lower quadrant. There was no history of

cancer in the family, of serious illnesses, nor appreciable loss in weight.

The patient had grown weak and was easily exhausted (how many would not be at the age of seventy-six?) and suffered cardiac distress. Had taken digitalis for many years.

Gross blood with clots was found in the urine at this time; frequency and dysuria were present.

*Examination of urine* revealed 70 mg. of albumin together with blood and pus.

*Blood pressure:* 150/74.

*Blood:* Blood urea nitrogen: 22 mg. per 100 c.c. of blood. Red blood cells: 5,000,000. Hemoglobin: 90 per cent. Leucocytes: 12,000. Polymorphonuclears: 78 per cent.

*Cystoscopic Examination:* The bladder was lavaged free of clots and found to be negative. Gross blood was seen exuding from the right ureter. The function of the left kidney was normal; there was complete absence of function of the right kidney.

*Right pyelogram* showed tremendous hydronephrosis, hydroureter, kinks and angulations of the ureter. A filling defect was seen in the lower third of the right ureter, suggestive of tumor.

*Impression:* Hydropyonephrosis of the right kidney. Hydroureter, kinks and constrictions. Possibility of ureteral tumor.

*Suggestion:* Two-stage ureteronephrectomy.

*Operation: Right nephrectomy:* Under spinal anesthesia the kidney was exposed and found to be the size of a grapefruit. Many adhesions were encountered. The ureter was fully 1½ inches in diameter. There was about one pint of purulent urine in the kidney. The kidney and upper third of the ureter were removed. He had an uneventful postoperative recovery.

*Pathologic examination* showed the kidney to be typical of hydropyonephrosis. There was no evidence of malignancy in the kidney.

*Subsequent Course:* For six months after the nephrectomy the patient passed no blood at all and seemed to be improving nicely, when suddenly blood appeared in the urine, and at cystoscopy it was found to come from the ureteral stump.

*Second Operation:* The patient was readmitted to the hospital and under spinal anesthesia the remaining portion of the ureter was completely removed through a rather long right McBurney incision. The ureteral stump measured about 1 inch in diameter, was thickened, and when opened was found to be filled with a purulent and bloody discharge. Attached to one side of the ureteral wall and hanging from its pedicle was a tumor the size of a hulled walnut, typical of papillary carcinoma. The patient made an uneventful recovery and left the hospital on the fifteenth postoperative day.

*Pathologic Report:* Examination of the ureteral stump revealed a tumor mass firmly attached to the lining of the ureter.

*Microscopic Diagnosis:* Papillary carcinoma of the ureter.

*Comment:* 1. The patient is alive, in excellent health, about eleven months after removal of the cancer-bearing ureteral stump. He shows no evidence of malignancy, has gained in weight and is happy in every regard.

2. This case seemed ideally suited to the two-stage ureteronephrectomy under spinal anesthesia because of the patient's age and severe chronic heart condition.

## SUMMARY

1. Cystoscopy and uretero-pyelography are of extreme importance to diagnosis.

2. Careful interpretation of *x*-ray plates is essential, especially as regards filling defects. It is often desirable to repeat the roentgen examination.

3. Pain, if present, is usually due in the earlier stages to back pressure caused by faulty drainage. In late stages it may be due to nerve impingement.

4. Hematuria is inconstant; it may be microscopic or macroscopic. One cannot rely upon the presence or absence of blood as an aid to diagnosis. It is merely a symptom to be analyzed.

5. Searching for atypical cells in the urine following ureteral catheterization may be helpful, but seems to be more theoretical than practical. They were searched for but not found in the 2 cases here reported.

6. These 2 cases show two varieties of carcinoma, one adenocarcinoma, the other papillary carcinoma. The latter is the

most frequently found variety of primary carcinoma of the ureter. The former is rare.

7. The two-stage nephro-ureterectomy carried out in one of my cases seems proper and safer, especially in patients with complications over which we have little or no control.

8. Every case of carcinoma of the ureter deserves to be thoroughly studied and given to the literature, in the hope that with accumulated experience earlier diagnosis may become more frequent, with more effective treatment as its corollary.

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CLINICAL-PATHOLOGICAL ASPECT OF

# INTESTINAL FIBROMATOSIS*

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## INTRODUCTION

INTESTINAL fibromatosis may be defined as a non-specific chronic inflammatory process of the gut wall with an unusual development of fibrous tissue, resulting in marked palpable thickening of the affected intestinal segment and a more or less pronounced degree of annular or tubular stenosis. The fibroplastic process affects principally the colon although, in a few instances, identical lesions have been found in the small intestine and stomach. This condition of tumor-like, unrestrained production of fibrous granulation tissue in the bowel is clinically often mistaken for the so-called hypertrophic form of tuberculosis or carcinoma. It may also be confused with intestinal lymphosarcoma, abdominal Hodgkin's disease, and intestinal blastomycosis, all these conditions more or less resembling each other in the clinical symptoms of tumor-like palpable masses with subsequent obstruction of intestinal passage. Moynihan called the process a "mimicry of malignant disease."

Fibromatosis of the colon as a clinical-pathological entity is briefly discussed in Boyd's "Surgical Pathology."[1] The index to the Surgeon General's Library and the current indexes to medical literature do not list the disease under this term. Literature on this subject is found under the term "non-specific infectious granuloma" of the intestine. Some of the recent publications dealing with this condition are given in the bibliography for further information.

The cases previously reported in the literature essentially answer the description of bulky masses of fibrous granulation tissue encroaching upon the lumen of the intestine with resulting obstruction. The chronic inflammatory nature of the process raises the question of its etiology. Mock[8] mentions appendicitis, diverticulitis, mucosal ulcers, foreign bodies, purse-string sutures, and tears of the mesentery as possible causes. In quite a few cases, however, the exact mode of infection could not be ascertained. One is impressed by the uniformity of the pathological-anatomical findings contrasting with the diversified clinical history. Granting that chronic irritation of the bowel and mucosal inflammation act as primary cause and port of entry for the infection, one is puzzled by the fact that only a small percentage of patients suffering from the lesions listed respond to the infectious stimulus with excessive piling up of fibrous tissue. To explain the fibrous overgrowth in certain cases, it seems reasonable to assume a *constitutional factor* in addition to the external factor of infection. The development of any marked degree of fibromatosis is determined by the individual tissue reaction rather than by the infection itself. Hayes[6] emphasises the scar-forming tendency of the Negro race. While this is generally recognized, I do not see any reason to exclude the possibility of certain individuals of the white race acting similarly. Reynolds[10] introduced the conception of "fibrous diathesis" as an inherent constitutional state in which the individual affected is predisposed

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to an unusual development of fibrous tissue at the site of previous irritation and inflammation. Such a congenital tendency

Fig. 1. Case IV. Gross appearance of resected ascending and part of transverse colon.

towards fibrous overproduction might manifest itself elsewhere in the body but in some way the intestine seems, besides the skin (keloid-formation), to be a site of predilection.

I would like to advocate the use of the term "fibromatosis" instead of infectious granuloma because emphasis is laid in this term on the fibrous overgrowth as the essential feature whereas granuloma sounds to me indefinite.

I feel justified in reporting briefly 4 cases of my own experience in addition to those published by other observers because of their unusual clinical and pathological aspect. The pathological findings as well as abstracts of the clinical data are given for correlation.

## REPORT OF CASES

Case 1. Mrs. M. S., aged fifty-eight, colored, housewife.

*History:* Usual childhood diseases. Pneumonia and pleurisy in 1918. No operations. Suffering from headaches and easily fatigued for several years. Gradual loss of anal sphincter control in the last few weeks. Pain over maxillary sinuses. Increasing intestinal obstruction.

*Clinical Data:* Admitted to hospital August 4, 1932. Eyes blurry. Conjunctival discharge. Tenderness over maxillary sinuses. Inflammation of throat and uvula. Lungs negative. Heart action rapid and bounding. Abdomen: large sinus tract on right side of rectum leading to an ischiorectal abscess with skin and tissues around it inflamed.

X-ray: osteomyelitis of lower border of sacrum.

Surgical: August 15, extirpation of rectal fistula. September 29: curretage of coccyx and sacrum. November 8: biopsy taken from site of old fistulous tract; histological examination revealed a non-specific chronic inflammatory tissue. November 15: left lateral colostomy performed; transverse pelvic incision made to explore. Diagnosis of *possible tuberculosis* made. Temperature fluctuated between 100° to 103°F.

Laboratory Data: Smears from rectal fistula were negative for acid-fast bacilli and gonococcus Kahn test negative. Albuminuria. Blood count: R.B.C. 3,700,000, Hgb. 60 per cent, W.B.C. 10,000 with 67 per cent polymorphonuclears.

Expired November 15, 1932.

*Autopsy Findings:* Pelvic topography: Pelvis was filled out by a matrix of fibrous and fat tissue which fused the anterior rectal wall together with the posterior vaginal vault. Cicatricial tissue encircled and compressed the rectum all around, converting it into a straight, firm, non-compressible tube with the lumen narrowed to a diameter of 0.5 cm. A jejunal loop was drawn downward into the space of Douglas and incorporated in the massive fibrous pelvic tissue. Upon dissection, it appeared to be adherent to the rectum at a point 6 cm. above the anus and communicating with the rectum (rectojejunal fistula). The tubular cicatricial thickening and constriction of the

rectum extended upward as far as 16 cm. from the anus.

Examination of the other organs revealed: osteomyelitis of the sacrum with formation of multiple fistulous tracts opening into a large decubitus in ischiosacral region; marked fatty infiltration of liver; brown atrophy of heart; left adhesive pleurisy; splenic atrophy; parenchymatous degeneration of kidneys with chronic interstitial inflammation.

Microscopical study of rectal wall and pelvic tissue: Mucosa gone and replaced by a fibrous granulation tissue rich in fibroblasts and chronic inflammatory cells. Remainder of rectal wall partially fibrosed and infiltrated with dense collections of wandering cells, plasma cells, and lymphocytes. Outer coats merge insensibly with the dense pelvic connective tissue which likewise exhibits focal infiltration with chronic inflammatory cells. No evidence of a malignant or tuberculous process. From the gross and microscopical findings, the diagnosis of the rectal condition was "chronic inflammatory tubular-stenosing fibromatosis, associated with chronic suppurative periproctitis and osteomyelitis of the sacrum."

Case II. Mrs. H. D., aged seventy-three, white, housewife.

*History:* Bowels always constipated; had to take frequent laxatives and enemas. Her condition became suddenly aggravated in July, 1933. Since then, she has been more and more constipated, felt general abdominal aches, and lost 20 lbs. History obtained with difficulty because of deafness of patient.

*Clinical Data:* Admitted to hospital November 11, 1933.

Physical examination: Toothless. Tongue heavily coated. Hard of hearing. Pulmonary and cardiac findings negative. Abdomen thin-walled with skin loosely applied. No tenderness or rigidity made out. Outline of cecum easily found; appeared like a firm circumscribed mass giving gurgling sounds upon moving it. Peristalsis felt.

Proctoscopy: Scope could not be passed beyond a point 4 inches above anal orifice. Findings verified by *x*-ray.

Laboratory Data: Urine analysis insignificant. Kahn test negative. Blood count: R.B.C. 4,500,00 Hgb. 81 per cent, W.B.C. 9,800 with 69 per cent polymorphonuclears.

A tentative clinical diagnosis of *rectal carcinoma* was made.

Expired November 11, 1933.

*Autopsy Findings:* Abdominal cavity: There was a chronic adhesive peritonitis resulting into adhesions between liver and transverse colon, liver and right kidney, left adnexae and sigmoid, gall bladder and small intestine. The right adnexae were thrown up to the ileocecal junction by firm fibrous adhesions, and the appendix was incorporated in this adhesive mass. At one particular point in this mass close to the ileocecal valve, on slight traction, the ileum was ruptured and a fecolith about 3 cm. in diameter was expelled. Upon dissection, the terminal ileum segment was found to be hyperemic, thick-walled, and fibrosed with the mucosa in places herniated through the muscularis forming several small outpocketings filled with retained fecal concretions. The ileocecal passage was narrowed and nonelastic due to the ring-like induration of the intestinal wall. The appendix was thick-walled and firm with the lumen narrowed and empty, and blending into the bulky fibrous adhesions. The large intestine was small in caliber and contained a small amount of semisolid fecal matter. The pelvic colon and rectum were immobilized by fibrous adhesions but otherwise soft and collapsible with no strictures found on section, and showed a series of small diverticula. The mesentery of the small intestine showed enlarged lymph nodes, not indurated.

Examination of the other organs and structures revealed as principal changes brown atrophy of heart, chronic cholecystitis and cholelithiasis, atrophy of the liver, spleen, and kidneys, and fibrosis and atrophy of the internal genitalia.

Histological Study: The structure of terminal ileum segment was replaced by a fibrous granulation tissue containing great numbers of fibroblasts and mixed collections of lymphocytes and plasma cells, and well supplied with sprouting blood capillaries, merged with bulky fibrous and fat tissue around the bowel. The mucosa was completely gone. In the appendix, the glands of mucosa were atrophied, and the lymph follicles were gone. The submucosa was greatly thickened and densely fibrous. The muscularis was crowded with focal round cell collections and merged with inflammatory fibrous adhesions around the wall. Ingrown fat was enclosed in the muscularis.

Based on the gross changes as well as on the microscopical findings, the diagnosis was "stenosing chronic inflammatory fibromatosis of the ileocecal junction which developed

from a chronic recurrent appendicitis and periappendicitis."

Case III. Mrs. M. H., aged fifty-nine, white, housewife.

*History:* Had measles, mumps, and chickenpox in childhood. Had three children, first died when born. No previous operations. Past health in general has been good except for constipation in last thirty years and attacks of gas and constipation the last six months. In the last two months, there has been pressure on the urinary bladder.

*Clinical Data:* Admitted November 10, 1933.

Physical examination revealed: false upper teeth. Throat, eyes, ears, nose, and neck normal. Lungs clear. Heart slightly enlarged to the left; second aortic sound accentuated. Pulse at present regular. Abdomen flabby; tenderness over bladder on deep pressure.

Sigmoidoscopy showed an obstruction about 7½ in. above the anus. *X*-ray examination with barium enema verified this observation and revealed several irregular unfilled areas in lower sigmoid and 3 diverticula in upper colon. A tentative diagnosis of *cancer or diverticulitis* of the colon with inflammatory obstruction in the lower sigmoid was made.

Operation November 14, 1933; resection of sigmoid (Dr. L. Kinner).

Patient made an uneventful recovery and left the hospital November 29. Living and well at the time this paper was submitted for publication by communication of attending physician.

*Pathological Findings:* Indurated, thick-walled segment of sigmoid measuring 10 cm. in length and 6 cm. in diameter. Surface was rough from adhesions and covered with massive fat deposits. On section, there was seen a narrowing of the lumen to a diameter of about 0.4 cm., and a diffuse tubular fibrous induration of the wall the thickness of which varied from 2 to 3 cm. The mucosa was thrown into thick ridges and extruded in several places through the muscularis with the formation of small false diverticulae. A few scybala were retained in the mucosal pouches.

Microscopically, the structure of the sigmoid wall was dominated by a marked hypertrophy of the muscularis and conversion of the subserosa into a thick layer of fibrous granulation tissue containing an abundance of fixed connective tissue cells and sprouting blood capillaries, and exhibiting a diffuse infiltration with lymphocytes, plasma cells, eosinophiles, and polymorphonuclears. The lymphoid elements predominated among the inflammatory cells and formed in places circumscribed collections. The fibrous layer covered about half of the thickness of the wall and merged with fatty tissue around the bowel. The mucosa herniated in some areas through the muscularis.

In accordance with the gross and histological findings, the diagnosis was "stenosing inflammatory fibromatosis and peridiverticulitis of pelvic colon."

Case IV. Miss D. W., white schoolgirl, aged fifteen.

*History:* Had the ordinary diseases of childhood. Tonsillectomy 1928. Otitis media 1931. Appendectomy 1930; appendix in the surgical and pathological record described as gangrenous. Has always been a healthy active child until August 1932 when she was taken sick with diarrhea and colicky pains in right lower abdomen. Since that, she had suffered from recurrent attacks of alternating constipation and diarrhea and frequent discharge of liquid, sometimes mucous stools. Often nauseated and occasional vomiting. Lost gradually in weight. No menses yet.

*Clinical Data:* Physical examination in the summer of 1933 revealed a poorly developed, undernourished emaciated child appearing younger than stated age of fifteen. Head and chest findings were essentially negative. Abdomen was scaphoid in type and thin-walled; marked tenderness and rigidity over right lower quadrant. No definite masses felt. External hemorrhoids seen. *X*-ray department reported evidence of multiple strictures in the colon. Discharged in slightly improved condition September 8, 1933.

Readmitted October 1933. *X*-ray examination was repeated and a tentative diagnosis of circular malignancy or granulomatous formation made. Exploratory laparotomy performed. Surgeon described a tumor mass encircling the cecum and transverse colon near the hepatic flexure. No attempt was made to remove the mass in whole or part. Clinical condition remained unchanged except onset of slight fever between 100° and 102°F.

Laboratory Findings: Stools negative for parasitic ova and bacilli of the typhoid-paratyphoid group. Leucocytosis fluctuated between 9,000 and 16,000 with 75-78 per cent polymorphonuclears. R.B.C. around 4,000,000. Hgb. 70–74 per cent. Blood urea 12 mg., blood sugar 98 mg. Blood cultures sterile. Occult blood in stools found. Urinary findings negative. Marked hypochlorhydria of gastric juice.

Sent home November 4, 1933.

Readmitted January 4, 1934. Failed to

improve at home. Sigmoidoscopy showed numerous punched-out ulcers of the mucosa. Preoperative diagnosis of *malignancy or tuberculosis* made.

January 6: Operation (Dr. E. Bush). Resection of ascending colon and part of transverse colon performed followed by ileocolostomy. Patient made an uneventful recovery and gained in weight.

*Pathological Findings:* Resected ascending and transverse colon measuring 22 cm. in length and from 4 to 6 cm. in transverse diameter. Shrunken and converted into a thick-walled, firm, non-elastic tube. Serous coat roughened from dense fibrous adhesions. Wall exhibits throughout a marked tubular fibrosis, measuring in thickness from 1 to 2 cm. A walnut-sized false diverticulum formed by herniation of the mucosa through the muscularis is found about 7 cm. above the proximal end. The lumen is narrowed to a diameter of 0.5 to 1.0 cm. but patent. Mucosa below the diverticulum is smooth; above it, it is thrown into thickened nodular folds. Microscopically, the structure of the wall is dominated by a tremendous thickening and inflammatory fibrosis of the outer coats. Mucosa shows glandular hypertrophy. Lymph follicles in the submucosa are prominent. From the submucosa, there spreads a diffuse and very dense infiltration with lymphocytes, plasma cells, polymorphonuclear and eosinophilic leucocytes in varying proportion through the muscularis and the subperitoneal coat, the latter insensibly merging with thick layers of proliferating fibrous granulation tissue which encircles the bowel. This granulation tissue is hyperemic, richly supplied with sprouting capillaries, and shows various degrees of fibrosis, densely fibrosed and cicatricial areas alternating with areas of loose edematous texture. There is no evidence of a malignant or tuberculous process. Pathological diagnosis: "chronic-inflammatory stenosing fibromatosis of ascending and transverse colon."

## COMMENT

The examination of the cicatrized intestinal segments in all 4 cases revealed a striking similarity of the microscopical picture which justifies their classification as the same end-process of non-specific inflammatory fibrosis. Giant cells, mentioned by Erdmann,[3] Golob,[7] and Wilinski[11] as frequently occurring, were not found. The fibrous overgrowth principally involved the outer coats of the intestinal wall, especially the subserosa. The structural uniformity contrasts against the diversified clinical data although the latter show certain points in common. Increasing constipation, abdominal pains, gas-attacks, and development of palpable masses were prominent in all 4 cases.

A previous appendicitis and perityphlitis as primary cause of the progressing fibromatosis is very probable in Cases II and IV. Two years' interval (Case IV) are not a point against it in considering that an encircling intestinal fibromatosis spreading upward as far as to the transverse colon is a very slowly developing process requiring a long time. The exact duration of the disease in Case II could not be determined because of lack of clinical history. The original mode of infection remained obscure in Case I; the fibrous tubular stenosis of the rectum was complicated by active suppuration in the perirectal tissues with fistula formation and sacral osteomyelitis. The jejunorectal passage contributed to the patient's dehydration and emaciation. In Case III, the fibroplastic process was apparently secondary to the diverticulitis.

A comparison between the anatomical findings and the tentative clinical diagnoses illustrates the great difficulty to recognize the true nature of the condition. Except in Case III where a preoperative diagnosis of diverticulosis had been made, diagnoses of tuberculosis (Case I), carcinoma (Case II), and malignancy or tuberculosis (Case IV) were submitted to me. In many cases, diagnosis will be impossible without the aid of biopsy. The erroneous diagnosis of rectal carcinoma in Case II, based on the proctoscopic findings, found its explanation in the kinking and immobilization of the rectum by pelvic fibrous adhesions binding it to the granulomatous mass at the ileocecal junction.

## SUMMARY

1. The definition of intestinal fibromatosis was given and its general pathology, etiology, and differential diagnosis were briefly outlined.

2. The clinical and pathological findings in 4 cases were presented.

[For References see p. 567.]

# ROENTGEN-RAY STUDY OF PERSISTENT ABDOMINAL FISTULAE

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WHILE it is usually presumed that an artificially created fistula represents a smooth tube-like tract, the instillation of an opaque contrast medium (iodized oil) reveals, as a rule, numerous accessory pockets and other circuitous routes communicating with the main fistulous tract.

FIG. 1. Case I.

FIG. 2. Case II.

These findings probably account partly for the trying experiences of surgeons in their attempts to repair these chronically persistent umbilicated craters.

CASE I. A woman, thirty-seven years of age, was admitted to Bellevue Hospital with severe epigastric pains which had persisted, with slight remission, for three days prior to admission.

Physical examination revealed an obese woman, slightly jaundiced, temperature 103°F., pulse 120, and respiration 24. The abdomen presented a slight fullness in the right hypochondriac region; there was also marked tenderness and some rigidity below the costal margin.

The cytological examination disclosed 11,700 leucocytes, 97 per cent polynuclears and 75 per cent hemoglobin.

Laparotomy revealed a tense and distended, scarred gall bladder containing black bile and several small calculi. There were no stones palpable in the common bile duct. A cholecystostomy was done and a number 16 F. catheter was inserted for drainage.

Three weeks later, the fistula was still present and draining. The instillation of iodized oil revealed a distorted gall bladder

with several accessory pockets which retained the opaque medium, and a dilated cystic and common bile duct which permitted the injected fluid to flow into the duodenum.

Case II. A man, fifty-five years of age, was admitted to a hospital on January 30, 1934 because of a sudden sharp pain in the right upper quadrant, tenderness and rigidity.

The operative findings were as follows: "A massive blood clot was found on opening the peritoneum which seemed to fill about half of the abdominal cavity, extending from the liver to a point two fingers below the umbilicus on the right side, and on the left to the nipple line. The exact origin of the hemorrhage could not be determined but it appeared to have come from the second portion of the duodenum or from the liver."

The patient was in extreme shock during and after the operation. Several small transfusions were given for several days. The patient finally recovered, after a rather stormy period. He was admitted to Bellevue Hospital two months after the exploratory laparotomy with a persistent fistula in the right upper quadrant.

The injection of iodized oil revealed a large pocket behind the liver communicating by a circuitous canal with what appeared to be a deformed gall bladder. The sinus tract, further outlined by the contrast medium, could be identified as representing the cystic duct, common bile duct and finally the iodized oil was seen to flow into the second portion of the duodenum.

### COMMENT

These cases represent a not very uncommon finding but vividly depict, by this special study with the opaque contrast medium, the dilemma which usually confronts the surgeon.

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* Continued from p. 565.

# HEMATEMESIS DUE TO TRAUMA OF THE LIVER*

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HEMATEMESIS occurs with such frequency that its usual causes are common knowledge. Ordinarily only lesions involving the upper gastrointestinal tract are considered in the differential diagnosis of this symptom. To this practice may be ascribed occasional errors in diagnosis. The purpose of this paper is to report an unusual cause for hematemesis and to call attention to similar infrequent causes.

## CASE REPORT

D. S. No. 17598. A sixteen-year-old schoolboy was admitted on April 8, 1933 complaining of pain in the right shoulder of three hours' duration. He stated that while running he fell against a curbstone, falling on the right upper abdomen and on the lower right chest anteriorly. This was followed immediately by pain in the right upper quadrant and in the tip of the right shoulder. The pain was constant, and associated with progressive weakness.

*Physical examination* revealed an acutely ill boy with marked pallor of the skin and mucous membranes. The extremities were cold and clammy. There was a red welt extending across the lower anterior portion of the right chest and the right upper quadrant. The abdomen was slightly distended and there was tenderness and spasm in the epigastrium and in the right upper quadrant. There was marked tenderness in the right costovertebral angle. The temperature was 100°F., pulse 104, respirations 28, B.P. 120/70. The examination was otherwise negative.

*Clinical Pathology:* The white blood count was 21,000; Hb. 90 (T.); red blood count 4,100,000. The urine contained a slight trace of albumin and 30 red blood cells per high power field.

Diagnoses of ruptured liver, ruptured right kidney, ruptured viscus, and intraperitoneal hemorrhage were made. Because of the possibility of ruptured viscus, laparotomy was performed shortly after admission. Under general anesthesia the abdomen was opened through a high right paramedian incision. Exploration revealed a large amount of free blood in the peritoneal cavity. There was an oblique tear through the upper surface of the right lobe of the liver corresponding in direction to that of the overlying rib. The tear was very superficial laterally, but deep medially. There was edema of the gastrohepatic omentum. A slight rupture of the lower pole of the right kidney with a moderate intracapsular hemorrhage was noted. The tear in the liver was packed with gauze and the abdomen was closed. Convalescence was not remarkable except for nausea and epigastric pain both of which were fleeting in character. On two occasions the icteric index was 17.5 and the skin and sclerae showed slight icterus which was not adequately explained. The patient was discharged well on the thirteenth postoperative day. Two weeks after discharge he returned to the emergency ward complaining of severe pain in the right upper abdomen associated with vomiting. He stated that the vomitus contained about one teaspoonful of bright red blood. Physical examination was negative, and after brief observation he was again discharged. One week later because he continued to complain of epigastric pain, nausea, and of several dark-colored stools, he was readmitted to the hospital. At this time physical examination revealed the following: pallor and dehydration, slight epigastric tenderness, B.P. 80/45, T. 99.2, pulse 120, respirations 20. Clinical Pathology: urine negative, white blood count 33,800, Hb. 90 (T.), red blood count 6,100,000. The stool was grossly bloody.

On the day of admission he suddenly vomited about a liter of bloody material and went into shock. He was put on a Sippy regime. Ten days after admission a partial gastrointestinal series revealed marked pylorospasm. The

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duodenal cap was spastic, irritable and irregular. The roentgenologist's opinion was that the patient had a duodenal ulcer, which, were it

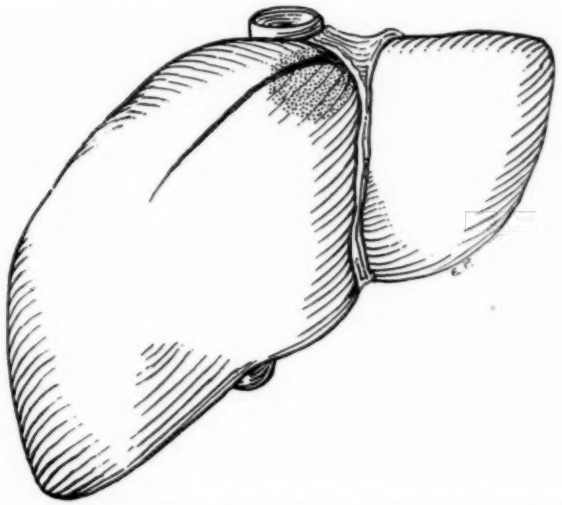

Fig. 1. View of whole liver showing extent and course of tear.

not for the recent history, could be reconciled with the clinical findings. He appeared well for another ten days, when he had a second severe hematemesis and again went into shock. He responded well to the usual treatment until four days later. At this time, because of a recurrent massive hemorrhage from what was apparently a duodenal ulcer, he was subjected to laparotomy. Exploration revealed the liver to be normal except for adhesions over the upper surface. The stomach was opened, and both the stomach and duodenum were very carefully examined. No ulcer, or any other cause for hematemesis was found. The stomach was closed and a jejunostomy was made for feeding, and the patient was transfused at the close of the operation. His convalescence was stormy. He vomited all oral and jejunostomy feedings and, in addition, on the eighth postoperative day he vomited about 50 ounces of bloody fluid. He recovered after strenuous treatment and slowly improved during the following three weeks. The jejunostomy tube was then removed, after which he tolerated a soft diet with only occasional attacks of vomiting. The vomitus was frequently blood streaked. On the thirty-second postoperative day he twice vomited bloody material, the total volume being about 50 ounces. On the thirty-sixth postoperative day he was esophagoscoped to determine whether or not any esophageal lesion might be the cause of the repeated hemorrhages. The examination revealed the esophagus to be normal. Three days later, on the thirty-ninth postoperative day,

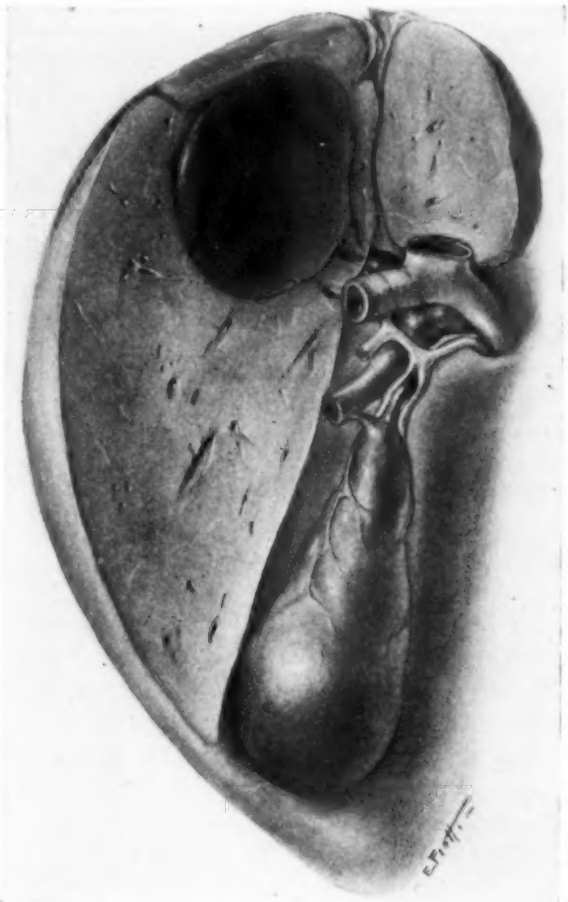

Fig. 2. Liver sectioned. Shows relation of tear to hematoma and relation of hematoma to branches of portal vein, bile ducts, gall bladder, etc.

he suffered another massive hematemesis. He was again transfused and operated upon. Minute search revealed no obvious cause for hematemesis. The liver appeared the same as in the previous exploration. Since the esophagus and the stomach were believed to be normal, it was assumed that the bleeding came, perhaps, from a small ulcer on the posterior wall of the duodenum, which could not be identified. The duodenum was therefore transected, both ends were closed and a posterior gastroenterostomy was made. At the conclusion of the operation his condition appeared fair, but he was transfused. On the fourth postoperative day he had another gastric hemorrhage, and from then on he went rapidly down hill. The wound separated on the fifth postoperative day, and he expired two days later.

Postmortem examination revealed the stomach to be normal except for the gastroenterostomy. The stump of the duodenum was dilated. No ulcer was found. The liver weighed 1320 gm. and was of normal color and consistency. There was a healed rent 10 cm. in length in the superior surface of the right lobe of the liver. The rent was oblique corresponding in contour to the curve of the overlying rib. The scar passed beneath the annular ligament and reached to the inferior surface of the liver in the region of the porta hepatis. Here it was found to extend into a well-defined cavity about 4 cm. in diameter which was partly filled with blood clot and communicated with a large branch of the portal vein, and a greatly distended bile duct. The gall bladder and biliary ducts were filled with clotted blood mixed with bile. Similar material was found in the duodenum and intestines.

## COMMENT

While the greater number of cases of hematemesis are caused by lesions located in the upper gastrointestinal tract, there are extrinsic causes not infrequently encountered. In discussing the diagnostic significance of hematemesis Rivers and Wilbur[1] state that 90.5 per cent of all cases of hematemesis are due to intrinsic gastroduodenal lesions; 5.1 per cent are due to cirrhosis and splenic anemia; and 4.5 per cent are due to all other causes, including cholecystitis, hemophilia, hemolytic icterus, and hemorrhagic purpura. In 2.2 per cent of the cases the cause is indeterminate.

It does not seem to be generally appreciated that disease or injury to the liver and bile passage may give rise to hematemesis. This fact, however, is demonstrated by the foregoing case and others found in a search of the literature.

The mechanism of the hematemesis in such cases varies somewhat with the nature of the lesion concerned. In our own case autopsy showed that the tear in the liver, which was at first thought to be superficial, extended deeply, and cut across not only a large branch of the portal vein but also a sizable bile duct. It is apparent that the blood found its way from the torn vein into the open bile duct, and thence into the hepatic and common bile ducts, the gall bladder and duodenum.

A few similar cases have been found in the literature. Thorlakson and Hay[2] report a case in which there was trauma to the upper quadrant pain, rigidity, tenderness and icterus. Much dark red blood was passed by bowel. Post-mortem examination disclosed partly healed wounds on the right lobe of the liver. In the center of the right lobe was found a large area of necrotic tissue. The hepatic, cystic and common ducts, as well as the gall bladder, were filled with blood and, in addition, much old blood was found in the peritoneal cavity. No hematemesis was noted in this case.

Jankelson and White[3] report a series of cases of hematemesis concomitant with gall-bladder disease. They describe 6 of their own cases and cite 12 others from the literature. In none of their cases, however, is it shown definitely that the bleeding came from the liver or bile passages. They explain the hematemesis by erosion of vessels in the gall-bladder wall, fistula formation, or hemorrhagic infarction of the gall bladder.

They also refer to Naunyn's theory that toxins in the blood coming from the infected gall bladder cause bleeding from the mucosa of the stomach or duodenum. Of the 12 cases which they cite from the literature, 3 are pertinent to this discussion. The first is a case reported by Schnyder[4] of a man who had a large intestinal hemorrhage. Autopsy revealed a gall bladder which had perforated and bled freely into the peritoneal cavity and intestine. The second is a case of Lobstein's[5] of a sixty-five year old woman with intestinal hemorrhage. At operation a perforated gall bladder was found bleeding into the peritoneal cavity and into the lumen of the gall bladder. The third case by Heuser[6] is of a woman with a large intestinal hemorrhage and slight jaundice. Operation showed hemorrhagic cholecystitis with

ulceration of the gall bladder and many stones. Autopsy nine days later revealed a hemorrhagic infarct of the gall bladder.

Nothnagel[7] states that in hyperemia and inflammation of the liver blood may be found in the bile passages and the gall bladder. Quinquad[8] cites a case of hemorrhagic cholangitis associated with blood in the bile ducts and intestines, resulting in bloody stools and hematemesis.

Finally, Taylor[9] reports a case of a man aged twenty-two who, after recovery from a severe gastric hemorrhage revealed at operation a hard mass, the size of a walnut, in the posterior wall of the duodenum. A gastroenterostomy was made. A month later the patient had another hemorrhage. Two months later a second operation revealed the duodenal mass to be much larger. At necropsy a ruptured aneurysm of the hepatic artery communicating with the gall bladder was found.


## SUMMARY

1. A case of hematemesis due to trauma of the liver is reported.

2. The mechanism of the hemorrhage is described.

3. A brief review of the literature is included.


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# SKIN-GRAFTING

## SUCCESSFUL OUTCOME DESPITE UNUSUAL DIFFICULTIES

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THE extraordinary conditions produced by the wounds sustained during the World War gave a great impetus to all branches of plastic surgery, which has ever since continued to exercise a decided influence upon the treatment of extensive denudations and disfigurements sustained in civil life.

No "rule of thumb" can be laid down for the handling of these cases. Each one presents considerations peculiar to itself, and the surgeon's past experience, while helpful in a general way, frequently gives him no assistance in solving any special problem. But the gradual accumulation of data concerning all phases of the question will be of great help to everyone interested in this type of surgery.

The case about to be reported presents several features so out of the ordinary that the writer feels it has an interest and value making it worthy of publication.

### CASE REPORT

A fat man, aged forty-six years, while at work on March 16, 1933, lacerated his left elbow. The next day the entire left arm was stiff, swollen and painful; there was a chill, followed by a rise of temperature to 104°F. and several vomiting attacks.

Admitted to Sydenham Hospital, March 22, 1933, he showed severe cellulitis involving the entire left forearm and lymphangitis up to the axilla. The skin was unusually thick and edematous, while the subcutaneous tissues and fascia had become necrotic. The small wound over the olecranon process was surrounded by a large phlegmon, extending from the lower third of the outer surface of the arm over the entire forearm as far as the wrist.

An attempt to establish drainage by making two deep incisions revealed the subcutaneous tissues yellowish-green in color, showing necrosis already established, the process having involved the aponeurosis.

The following day the wound was covered with a thick, cheesy exudate, but no fluid was draining from it. The application of 50 per cent Dakin's solution produced no apparent improvement. On the third day after the operation, the inflammatory swelling subsided somewhat and there was a profuse discharge of pus; but the patient became irrational and very restless, with incontinence of urine and flatus. The wound edges became gangrenous and were cut away with scissors; but continually larger areas were involved in the necrotic process, so that it was necessary to remove multiple sequestra of skin and fascia. On March 27 the general condition, both mental and physical, was much worse; but a demarcation line had become evident and there was a copious discharge of pus, ichorous in type. Culture of the pus on the third day showed Staphylococcus albus, the blood culture being negative.

During the following ten days there was slow but steady improvement. Large masses of necrotic tissue sloughed away and progressive gangrene of the skin continued. On April 9 the surface entirely denuded of skin measured 8 × 7 inches, while a smaller area, 1½ × 3½ inches, on the flexor surface of the forearm, was of a bluish-black color. This smaller area, however, did not slough and by April 13 had somewhat regained its normal color, so that there seemed to be hope that it would not become necrotic. Granulation now began. By May 14 the wound was clean and the cultures were negative. The patient, however, continued to be very irritable and extremely difficult to manage.

It was now decided to attempt to cover the large defect in the forearm (about 6 × 10 in.) with a skin-flap from the abdomen. May 16, 1933, just two months after the original injury, a flap measuring 5½ by 8 inches was raised upon the abdomen and its upper and internal

margins sutured to the upper and right cutaneous edges of the skin defect upon the forearm, the arm being immobilized against the chest

Fig. 1. Area of denudation; lateral view.

with strips of adhesive plaster. The following day the whole flap was of good color, and on the next succeeding day the portion nearest the wrist remained in perfect condition, although toward the elbow the skin was blistered and slightly discolored. By the 20th, about two-thirds of the flap appeared to have taken well, but the left side had not.

The patient was extremely uncomfortable and impatient, being much distressed by the inconvenience of the pinioned arm. His family added their entreaties that the arm be freed, and none of them could be brought to understand the necessity of permitting the collateral circulation to become established in the flap before it could safely be detached. Their refusal to cooperate finally compelled me to cut away the flap, although I felt certain that it would mean the complete failure of the plastic repair. The lower transverse margin of the flap rapidly necrosed and sloughed away; but, oddly enough, the central part grew and flourished and, under continuous dressings with wet saline solution, eventually healed the defect entirely, so that the arm now has perfect function and a fair cosmetic result.

The abdominal wound was covered by the French method of forming "sliding flaps" undermining the skin, drawing the flaps across the defect and suturing centrally and on both sides, so that the suture line, when completed, formed a letter H. A slight infection occurred at the left side of this repair; but, except for a small amount of seropurulent discharge, it gave no trouble and was perfectly healed when the patient was dismissed from the hospital, June 30, 1933.

Fig. 2. Area of denudation; anterior view.

## COMMENT

A search of the literature does not show any reports of cases closely analogous to this one. Indeed, our chief difficulty was a psychic one—the patient's extreme irritability and lack of cooperation. Tinker and Prince[1] many years ago reported a somewhat similar case, the covering of burns from exploding gasoline, sustained by a boy of twelve. They had to deal with a far larger area of cutaneous surface and extreme debility in their young patient, which made the use of flaps impossible at first. Later, the flap method was employed in part, reinforced by Thiersch grafting, with a final successful outcome. An extensive thesis on pedicle grafting of cutaneous defects of the hand was published by Keraudren[2] in 1922, but in

[1] Tinker, M. B., and Price, H. L. Modified autogenous grafting and turning skin flaps to cover granulating surfaces. *Ann. Surg.*, p. 849 (Dec.) 1911.

[2] Keraudren, J. A. V. Contribution a l'etude des greffes cutanees de la reparation des pertes de substances, etc. Bordeaux thèse, 1922.

none of his cases were the areas covered one half as extensive as that with which we had to deal, and he received better cooperation from his patients.

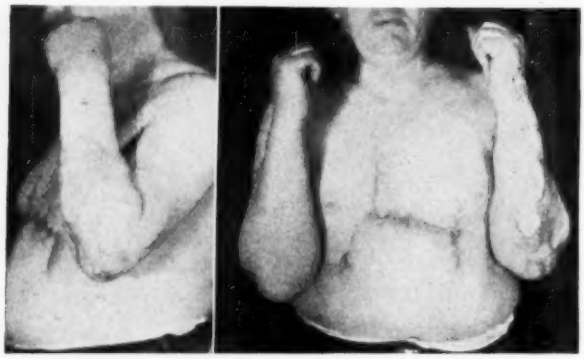

FIG. 3. FIG. 4.

FIG. 3. Healed graft and abdominal wound; lateral view.
FIG. 4. Healed graft and abdominal wound; anterior view.

In our case the behavior of the wound itself merits some study. It appears most surprising that a staphylococcus infection of no greater virulence than was demonstrated by our pathological examinations should have been solely responsible for such extensive destruction of tissue. It is the writer's belief that the thrombosis of the vessels, which was the direct cause of the wide extension of necrosis, was not so much of infectious origin as a *pressure necrosis* brought about by the weight of the affected tissues in the immediate vicinity of the original wound. It is also surprising that such a tremendous toxemia, sufficient to induce mental disturbance, could have arisen from a small wound and relatively low grade infection. The eventual happy ending illustrates what may sometimes be accomplished, even under the most adverse circumstances.

## SUMMARY

A case is reported of successful skin-grafting of an extensive area of denudation of the elbow and forearm following a laceration with infection. The defect was covered with a skin flap measuring 5½ × 8 inches raised upon the absomen, the arm being immobilized against the chest. In spite of the fact that the patient insisted on having the graft separated from its anchorage before it had taken completely, the end result was successful.

# KRUKENBERG TUMOR OF THE OVARY*

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ALTHOUGH there have been quite a few cases of this tumor reported in the literature, a detailed report of 2 more cases at this time would not be amiss.

Friedrich von Krukenberg,[1] in 1896, reported 5 cases of solid tumor of the ovary with a detailed description of the gross and microscopic appearance, making a definite differentiation between this growth and the ordinary types of ovarian malignancy. He called his growth "a fibrosarcoma ovarii mucocellulare" (carcinomatodes) which name shows that he considered his tumor primarily a fibrosarcoma with elements in its structure resembling carcinoma. He described it as a solid tumor of the ovary, usually bilateral, associated with ascites, characterized by a general growth of the whole ovary and usually free from adhesions. He described the histological picture as that of a stroma of fibrosarcoma enclosing in its meshwork the characteristic cells or group of cells which identify it. These are large, swollen cells with a mucoid protoplasm and with a nucleus often displaced eccentrically to form the signet ring appearance. He believed the tumor to be primary in the ovary.

Fallas,[2] quoting R. H. Major, states that after a careful search in the literature he collected 55 authentic cases, including one of his own. His conclusions after a study of these cases were that the tumor is essentially a carcinoma containing elements of fibrosarcoma, that it is not often primary but usually secondary to carcinoma elsewhere, and usually to that of the stomach or intestines.

Wagner,[3] in 1902, reported a case of Krukenberg tumor in an old lady sixty-nine years of age. In this case, at autopsy he found a tumor the size of a fetal head, of both ovaries, the gross appearance of which resembled Krukenberg's description of his tumor. He also found a crater-like ulcer the size of a 25 cent piece in the pylorus with adherent omentum and generalized metastasis including metastasis even to both ureters and tubes. The microscopic picture of the stomach tumor was that of a scirrhous carcinoma with gelatinous degeneration. The same type of metastatic cells were found in the ovary, tubes, etc. The histological structure of a scirrhus explains the frequent finding that "the main mass of the ovarian tumor represents a richly cellular, more or less dense proliferation of the connective tissue of the ovary" and that is why these tumors have been called fibrosarcoma.

In 1904 Schenck described a primary Krukenberg tumor in a woman twenty-four years of age. Stauder, in the Wurzburg Clinic, in a study of 20 cases of sarcoma of the ovary, discovered 4 Krukenberg tumors, 2 of which were primary, that is their nature was undetermined, and there was no autopsy.

Schlauhaufer showed in 8 cases of carcinoma of the stomach and the ovary, 2 typical Krukenberg tumors. Seventy-nine cases of carcinoma of the stomach, intestines, bile ducts, accompanied by tumors of the ovary were all carcinoma. Therefore the author came to the conclusion that he had to deal with primary carcinoma of the gastrointestinal tract and secondary tumor of the ovary. They were frequently described as endothelioma but were actually a metastasis of the scirrhus from the stomach.

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Glockner, on a basis of 27 cases of ovarian carcinoma, came to the following conclusions:

1. Secondary carcinoma of the ovary is relatively frequent.

2. Most of the bilateral ovarian carcinoma is secondary, especially to a carcinoma of the scirrhous variety.

3. In affection of the abdominal organs the ovarian carcinoma is in a prominent number of cases not primary but secondary.

Oscar Pilano, also of Wurzburg, states that under the designation of endothelioma, frequently various forms of carcinoma were described. The author studied 2 cases operated in the clinic of Professor Ott. Both left the hospital as cured. They were not followed up. The author is convinced however that the tumor was secondary as there were marked gastrointestinal symptoms.

Marchand[5] describes a case of typical bilateral Krukenberg tumor in a young girl fourteen years old. At the operation there were no other lesions. Four months later she was discharged at her request. She had ascites, a double hydrothorax and died one month later. There was no autopsy. I believe the author was erroneous in coming to the conclusion that this was a primary tumor of the ovary as the mode of death can be described as due to probably a carcinomatosis since there are a great many cases of Krukenberg tumor on record in which the primary tumor in the gastrointestinal tract was very small and the secondary tumor large.

G. Sacerdote[6] reports a case of a woman aged forty-five in which he did a gastric resection. Eleven months later he removed an ovarian tumor the size of an infant's head. There were some adhesions and a typical Krukenberg picture. The author does not state which tumor was primary despite the fact that the stomach symptoms were present first. The microscopic picture of both tumors was the same. Gleize-Rumbal and Robert[7] examined 15 tumors of this type and found the microscopic characterization described by Krukenberg. In only 3 cases were they able to find more or less differentiation with glandular formation of the gastrointestinal type. They feel that other cases would have been found if the entire ovary were examined histologically. Condamin[8] presented the case of a woman forty-six years old. A pylorectomy was performed for pyloric obstruction. Diagnosis at the operation was ulcer but the microscopic examination showed a glandular inclusion of the submucous and muscular layer. She gained 35 pounds and felt well. Two years later a bilateral tumor of both ovaries filling the pelvis and lower abdomen was removed. There were no other tumors present. The site of the primary operation was negative and she apparently made an uneventful recovery.

Miner[9] had a patient aged nineteen with a tumor of the right ovary 2 inches in diameter. It showed the typical Krukenberg characteristics. There was no complete exploration of the gastrointestinal tract at the time of operation. She has been followed up and examined repeatedly for five years following operation and up to that time has remained in good health.

Jarcho[10] reports 7 cases. Six followed gastric carcinoma, 3 of which were solid tumors with mucous changes, one was a fibrous tumor showing mucous transformation. The author believes in his cases that the propagation of the tumors was through the lymphatics, probably by the following route: first, the retrogastric route, then the superior lumbar group, thence to the ovaries. He does not think that the implantation theory is important and concludes that a removal of the genital organs should be looked upon as a palliative measure. Guiroy and Jacob[11] report a case of a woman thirty-nine years old, four and one-half months pregnant with gastric symptoms, that is, coffee-ground vomitus etc., and two months later, fever, jaundice, melena, anemia, edema of legs and oliguria. She aborted and died eleven days later. Autopsy showed a perforative carcinoma of the stomach, a

Krukenberg tumor the size of an orange, and both showed a colloid carcinoma.

Bourg and Cordier[12] report a case of a woman fifty-two years old on whom they did a subtotal hysterectomy for fibroma and tumor of the right ovary and infundibuliform ligament. Four months later she developed intestinal obstruction with a generalized carcinoma of the intestine and stomach. There was no biopsy or autopsy. The authors, quoting Fraenkel, state "primary tumors of the ovary never form secondary lymphatic metastasis into the walls of the tube and uterus, whereas secondary Krukenberg tumors do." They recommend the following procedure in ovarian tumors:

1. Always examine the stomach in bilateral tumors.

2. If no other metastasis, remove the stomach tumor.

3. If the stomach is negative, remove the ovary if there are other metastases. If not, do a subtotal hysterectomy.

Babes and Pantz[13] report the case of a woman twenty-five years old with a tumor reaching to the level of the umbilicus. She had a generalized anasarca. The specimen was a typical Krukenberg tumor with a primary growth in the stomach. They do not attempt to explain the route of metastasis. Merken[14] reports the case of a woman aged thirty. At the age of twenty-four she had a gastric resection for a linitis plastica of ulcer origin. One and one-half years later she was operated on for an ovarian cyst (?). At operation they removed a solid tumor the size of a fetal head from the left ovary and a cystic right ovary. The tumor was a Krukenberg. The apparent gastric origin emphasizes the necessity for exploration of the gastro-intestinal tract in all solid tumors of the ovary.

Bennett and Douglass[15] report a case of primary jejunal annular carcinoma with a secondary Krukenberg tumor of both ovaries. Fallas reports 2 cases of Krukenberg tumor. The first patient was a woman forty-three years old. The ovaries were removed, a mass was felt in the stomach, but the stomach was not operated upon. She died four months later. No autopsy was performed. The second case was that of a woman forty-three years old. A double tumor was removed and no growths felt in the stomach. Four months later, on account of a rapidly growing tumor the left breast was removed and there were Krukenberg cells recovered in the breast tumor. Five months later the patient died with general carcinomatosis and apparent involvement of the lungs. There was no autopsy.

Case 1. Mrs. L. S., aged fifty-four, white, Hebrew, was first seen June 11, 1931 with the following history:

The patient was entirely well and free of symptoms until August, 1930 when she began to have heartburn, belching, epigastric fullness and distress followed by vomiting. These symptoms began fifteen minutes after eating and she thought certain articles of food were to blame. Vomitus consisted of food and gastric juice, and was never coffee-ground or bile-stained. Vomiting had occurred once daily for the past two months, usually after the evening meal. Now it is coffee-ground in character. No pain precedes or follows vomiting. Belching has also increased. She has lost 45 pounds during this period. Markedly constipated for the past three years. She has not lost her appetite but is afraid to eat on account of vomiting. Two months ago she was jaundiced for a period of two days. She believes it disappeared after a cathartic. No gross melena.

*Past History:* No serious illness. No previous operation.

*Menstrual History:* Uneventful. Menopause nine years previous. Ten pregnancies, seven children living, three miscarriages. All her deliveries were normal.

Her family history is negative.

*Pbysical Examination:* Heart and lungs entirely negative. To the right of the umbilicus is a mass the size of a lemon. The mass is nodular, hard but not tender. The right upper quadrant of the abdomen appears distended. The lower abdomen is flat. No ascites, no palpable glands. The liver edge is not palpable, neither is the spleen. Blood pressure 160/110. Urine examination shows a faint trace of albumin, otherwise negative. The blood shows

3,620,000 R.B.C., 67 per cent hemoglobin (Sahli). Wassermann and Kahn reactions were negative. The *x*-ray shows a pyloric obstruction

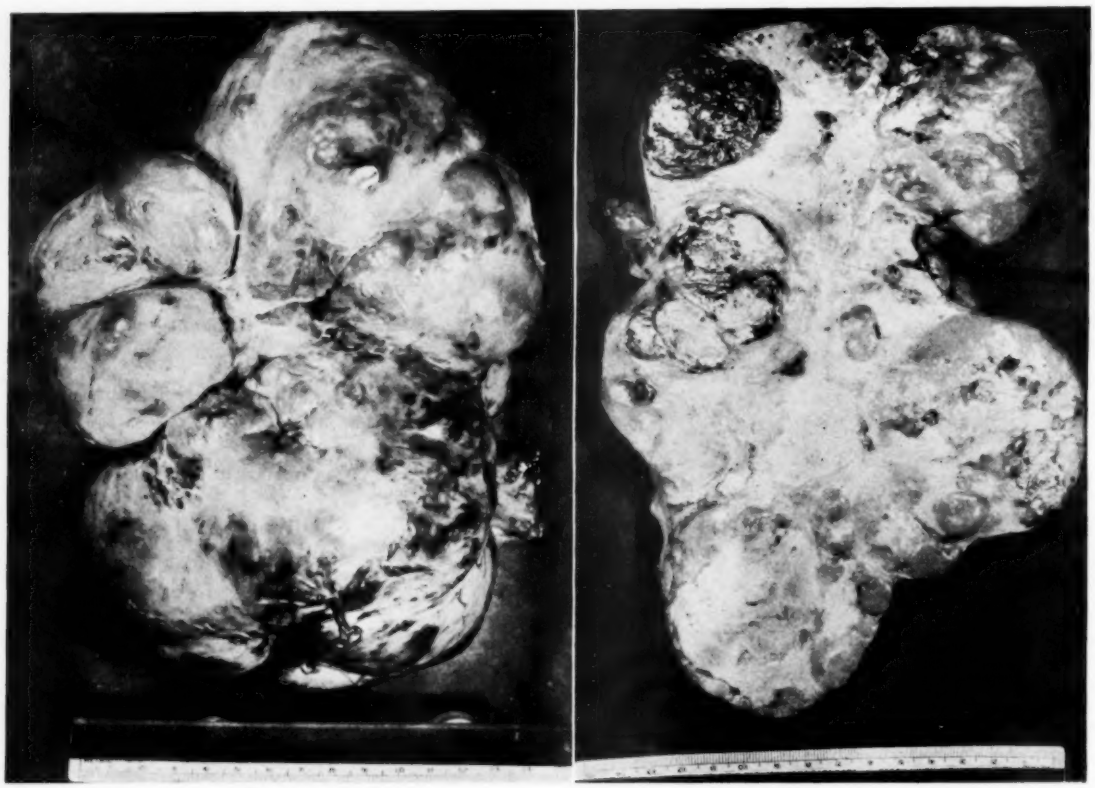

FIG. 1A. FIG. 1B.

FIG. 1. Case 1. A and B. Krukenberg tumor of right ovary. Gross specimen removed at operation.

with a scirrhous carcinoma.

*Operation* was performed June 13, 1931. Findings were a mass the size of a hen's egg at the pylorus. Several glands in the greater and lesser omentum. A cyst the size of a hazel nut on the posterior wall of the pylorus slightly adherent to the pancreas was found. No liver metastatis. Through a midline incision a typical Polya gastric resection was done dividing the stomach on the lesser curvature about 1 inch below the esophagus and on the greater curvature 1 inch to the left of the splenic artery. From this line down to and including 1 inch of the duodenum was resected.

*The pathological report* was as follows: Gross examination showed a section of the stomach consisting of the pyloric end, a part of the lesser and greater curvature measuring 14.5 by 6 cm. at its widest portion. Pyloric end is firm and feels almost like cartilage. The stomach has been opened along its lesser curvature previous to examination, exposing the interior of the stomach. The pyloric end shows a pale yellow, extremely firm infiltration which involves all coats of the stomach except the serosa.

Microscopic examination shows epithelial neoplasm in which the type of cell is that of a gelatinous cell carcinoma. This neoplasm invades the muscularis mucosa where there are many cell emboli seen in the lymphatics. The muscularis of the stomach is also invaded. There is a marked lymphatic reaction in the mucosa and muscularis. Diagnosis: Carcinoma of the stomach (gelatinous).

She was discharged from the hospital July 1, 1931 feeling and eating well. Fluoroscopy showed a well-functioning stoma. She was seen at intervals. On October 27, 1931 her weight was 119. She was feeling well and examination showed no masses or any evidence of metastasis anywhere. On April 4, 1932 she presented herself in the following condition: Weight 128, feeling well, but noticed a mass at the brim of the right pelvis about five weeks previously. This mass gradually increased in size, then appeared on the left side until it reached a level about 1 inch above the umbilicus. This mass was hard, nodular, not tender and freely

movable. No ascites was present. Bimanual examination showed the mass originated in the adnexa and filled the posterior culdesac.

a pale, smooth and glistening serosa. The uterus is firm in consistency. The cervical canal is closed at its external os and the cervix shows

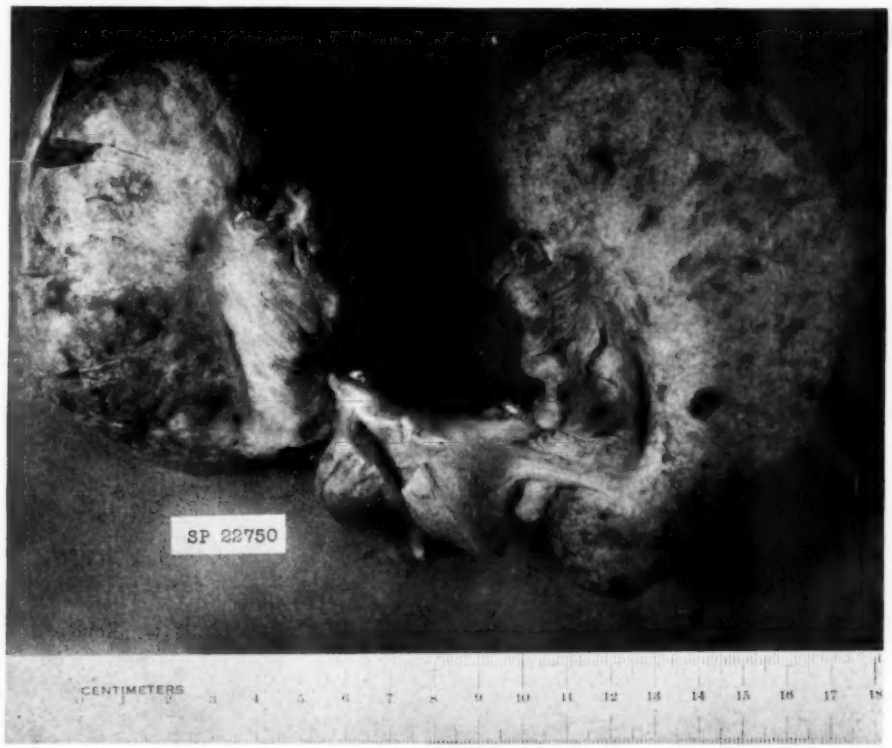


Fig. 2. Bilateral Krukenberg tumor of ovary. Gross specimen removed at operation, showing ovarian tumors.

She was admitted to the hospital April 28, 1932. Urine was negative except for a trace of albumin. Blood showed 3,550,000 R.B.C., 68 per cent hemoglobin. There was a slight achromia and polychromatophilia. There were 10,650 W.B.C., 76 per cent polymorphonuclears, with 2 per cent eosinophiles.

She was operated on April 30, 1932. The findings were a nodular mass the size of a small watermelon arising from both ovaries and fixed in the pelvis. The mass was adherent posteriorly to about 6 inches of sigmoid and anteriorly to two long loops of small intestine. Through a left paramedian incision beginning 1 inch above the umbilicus down to the pubis the entire mass consisting of both ovaries and uterus was removed en masse. Vagina was packed with iodoform gauze, abdomen closed with a drain inserted into the pelvis. The operative diagnosis was carcinoma of both ovaries.

*Pathological report* was as follows: Gross Examination: Shows the uterus with attached tube, ovary and broad ligaments. The uterus and cervix measure 10 × 6 cm. Body of the uterus is covered through most of its extent by evidence of increased fibrosis. The wall of the uterus measures 1 cm. in thickness. The uterine cavity is filled with a dark-brown thick chocolate substance. The uterine mucosa is pale, smooth and glistening. The attached tube measures 11 cm. × 5 mm. Its serosa is pale, smooth and glistening. The lumen is patent throughout. The ovary measures 3.5 × 1 cm. On section the ovary shows a marked increase in fibrous tissue. There is a large irregular globular mass measuring about 18 cm. in diameter. It is composed of a conglomerate mass of nodules which vary in size from that of a pea to that of an orange. The tumor is well encapsulated by a thick fibrous tissue. Some of the nodules are firm in consistency and others are soft and fluctuating. On section cut surface of the tumor shows many irregular areas of pale red and yellowish tissue surrounded by strands of dense fibrous tissue. Some of these islands of tissue are extremely hard in consistency. Others show marked evidence of degeneration and necrosis. Microscopic examination of the ovarian tumor shows a varied picture. In some of the sections there is a definite adenomatous

structure. The glands are irregular in size and shape and are surrounded by a fibromyxomatous structure. In other sections there is a

Fig. 3. Bilateral Krukenberg tumor of ovary, showing spindle cells with many large swollen cells containing globules of colloid gelatinous fluid. × 300.

diffuse cellular invasion suggesting a sarcomatous neoplasm. The cells for the most part contain vesiculary nuclei and in some instances have a definite signet ring appearance. The uterus, tubes and other ovary show no evidence of any malignant invasion and are the site of senile involutional changes. Diagnosis: Krukenberg tumor.

Patient remained well for eighteen months when she went down hill very rapidly with a recurrent carcinomatosis of the abdominal organs. Autopsy permission was refused.

Case II. An Italian girl, S. M., aged twenty-four, single, factory worker, was admitted to the hospital January 30, 1931 on the medical service with a diagnosis of pyloric obstruction. Her present illness began six months previous to admission. She vomited most everything she ate. After medical treatment vomiting subsided to the extent that she only vomited after a heavy meal. For a week previous to admission she vomited everything she ate or drank including water. Vomiting was preceded by a cramp but no nausea. She had a pain in the epigastrium which was relieved only by rest in bed.

*Past History:* Appendectomy eight years previous. Operated on for adhesions five years previous to admission. Relieved for one year.

*Menstrual History:* Puberty at fourteen, twenty-eight day type, four to six days' duration. Weight 94 lbs. Two months previous to admission she weighed 115 lbs. *X*-ray shows pyloric obstruction. Urine is negative. Blood shows 4,630,000 R.B.C., 80 per cent hemoglobin, 14,550 leucocytes, 82 per cent polymorphonuclear, 16 per cent lymphocytes.

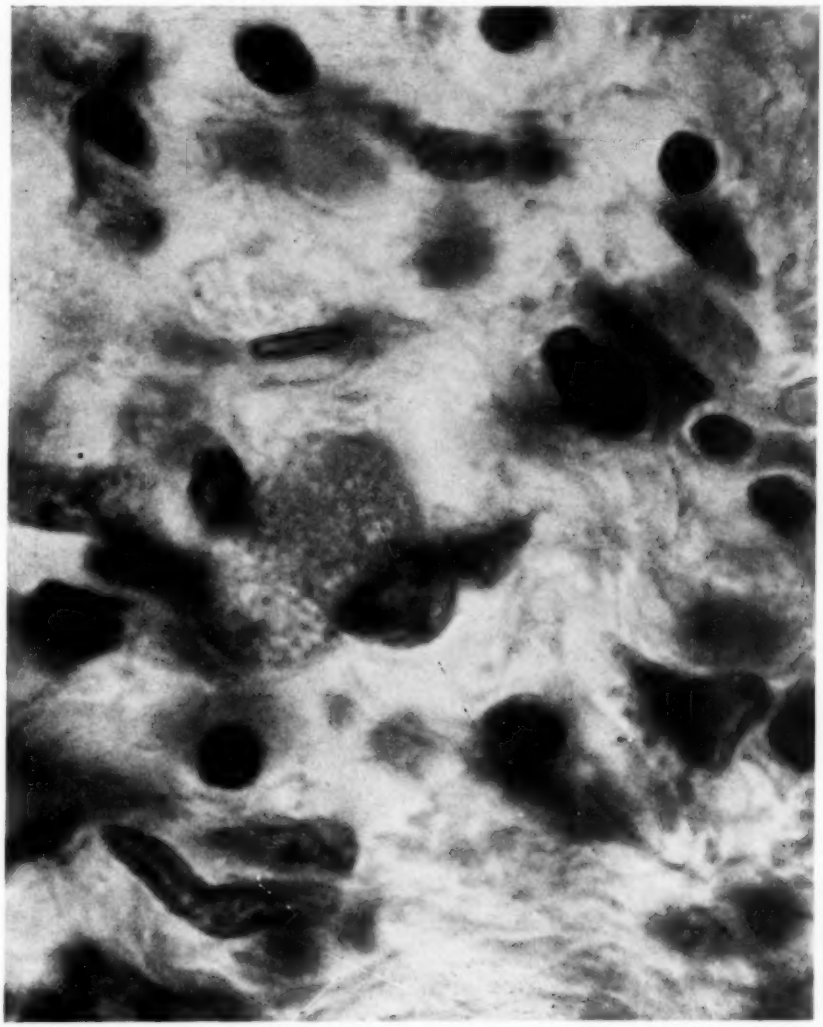

Fig. 4. Bilateral Krukenberg tumor of ovary, showing spindle cells with many large swollen cells containing globules of colloid gelatinous fluid. × 3000.

*Operation* February 2, 1931. Findings were a mass in the pylorus 4 inches long with a scar on the lesser curvature at the proximal end of the mass. There was no metastasis into the liver or surrounding glands. Through an upper right rectus incision 5 inches long a sub-total gastric resection was done using the Balfour modification of the Polya operation. Braun's entero-anastamosis completed the operation.

*Pathological report* was as follows: Gross examination showed pyloric end of the stomach containing markedly thickened and indurated pylorus. Serous surface was smooth, walls of the pylorus 1.75 cm. in thickness. On the lateral surface was a small ulcerated area. On the lesser curvature of the stomach on the pylorus is an ulcerated area 1 × 0.5 cm. The edges were indurated and ulcer appeared punched out. Base was covered by a roughened reddish surface. Rest of the stomach wall appeared thickened and mucosa was arranged in thick rugae. The entire specimen was 11 × 10 cm. at the distal end from the pylorus by 5 cm. at the pyloric opening. Microscopic Diagnosis: Linitis plastica (fibrous carcinoma).

On March 1, 1931 the fluoroscope showed a slow functioning stoma. She was discharged from the hospital March 3 in good condition,

eating well, no distress or symptoms. She was re-admitted to the hospital May 16, 1932 with the following history: For the past six months

Fig. 5. Bilateral Krukenberg tumor of ovary. Large cell with eccentric nucleus, seal-ring cell characteristic of Krukenberg tumor may be noted. × 4000.

there has been a return of some of her old symptoms, weakness, palpitation, dyspnea, loss of about 15 lbs. Three months previous to admission she noticed a mass in the right lower quadrant and five weeks before admission her abdomen began to swell and become continually larger. Seven months previous to admission her menstrual history was prolonged. She bled for seven or eight days, stopped for a day and then began to bleed again. This continued the following month and then ceased. For the past five months has had no menstrual bleeding at all. There was no hemoptysis, cough or night sweats. There were no symptoms directly attributed to stomach lesion.

*Physical examination* shows an anemic, emaciated young white female complaining chiefly of swelling of the abdomen. The abdomen was distended and tympanitic, a small amount of fluid in the dependent area giving shifting dullness. A ballottable bilateral mass arising from the pelvis was felt up to the level of the umbilicus. No tenderness or rigidity over this area. Bimanual examination reveals a mass originating from both sides of the pelvis. Uterus and cervix negative. Radiologic examination shows distal half of the stomach missing, drains normally, no six hour gastric residue. There is a large colonic residue in twenty-four hours. Urine negative. Blood showed 3,500,000 R.B.C., 45 per cent hemoglobin.

*Operation*, left rectus incision from 1 inch above the umbilicus to the pubis. About one gallon of straw-colored serous fluid evacuated. A tumor of each ovary was found, one on the left side one and one-half times the size of a man's fist, the one on the right side the size of a man's fist. There were no adhesions. The tumors were kidney shaped, smooth and outlined, solid and not lobulated. The uterus was small. The region of the primary growth was free of recurrence, liver negative. No palpable enlarged lymphatic glands in the abdomen or retroperitoneal space. Both tumors together with the tubes and body of the uterus were removed en masse. Abdomen was closed in layers without drainage.

Pathological report was as follows: Gross Description: Specimen consists of uterus and adnexae. The uterus is normal nulliparous organ and the adnexae show no inflammatory changes. Each ovary is replaced by a solid tumor of a meaty, firm consistency with a glistening surface. Both are attached to the broad ligament by the mesovaria.

The tumor of the left ovary measures 10.5 × 6.5 × 4.0 cm. in diameter, and the tumor of the right ovary measures 9.5 × 5.0 × 3.5 cm. On section both tumors are homogeneous, greyish pink in color with little evidence of increased vascularity and no necrotic or hemorrhagic areas. No ovarian tissue is recognizable to the naked eye.

Microscopic Description: Sections reveal three distinct types of tissue: a solid cell carcinoma, a myxomatous connective tissue, and tissue clefts lined by cuboidal flat epithelium. Carcinomatous areas consist of cells of moderate size with acidophilic cytoplasm and circular deeply stained nuclei of about half the diameter of the cell. Mitotic figures are rare. In this tissue many cells of another type are seen, viz: those with a large faintly granular

cytoplasm which is almost clear, containing an eccentric nucleus which appears to be superimposed on the outside of the cell (characteristic cell of Krukenberg tumor). The myxomatous tissue consists of an embryonal type of connective tissue which forms a supporting stroma in, and lies between carcinomatous areas. The tissue clefts are lined apparently by the thinned-out epithelium of the germinal layer of the ovary dipping down into the tumor. Diagnosis: Bilateral solid cell carcinoma of the ovary showing typical cells with eccentric nuclei characteristic of Krukenberg's metastatic ovarian tumor.

Patient left the hospital in good condition on August 22, 1932. In March, 1933 she was readmitted to the hospital with symptoms of acute intestinal obstruction. Exploration showed the entire peritoneum, intestines and liver to be studded with carcinomatous transplants. Several coils of small intestine were markedly adherent to the hysterectomy stump. These adhesions were liberated, relieving the obstruction. She survived the operation but died about six weeks later of cachexia. No autopsy was performed.

## SUMMARY

The following conclusions can be drawn:

1. Krukenberg tumors are essentially secondary to carcinoma of the gastrointestinal tract, usually the stomach, and most generally follow a scirrhous type of carcinoma.

2. In all cases of gastrointestinal malignancy in the female, the ovaries should be explored at the time of operation in addition to the exploration of the liver, mesenteric and retrogastric glands.

3. In all solid tumors of the ovary, the stomach and intestines should be explored.

4. If there is no general metastasis, both lesions should be removed even if it is necessary to do it in two stages.

5. These tumors should be regarded as fatal even though some of the patients are reported as well five years after operation.

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# EXPERIMENTAL INTRAUTERINE OVARIAN IMPLANTS PRESERVING THE NEUROVASCULAR PEDICLE

## CLINICAL SIGNIFICANCE*

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THE difficulty of obtaining accurate and complete data as to what occurs with human ovarian implants in the uterus, and the infrequency of pregnancy by present methods of implantation, led to experiments with rabbits to supplement present knowledge. At the suggestion of Dr. W. L. Estes, Jr., this work was done while serving as resident surgeon at St. Luke's Hospital, Bethlehem, Pennsylvania.

In the literature on transplantation or implantation of the ovary in the human uterus, two locations have been used mainly. In the first, the ovary is implanted well within the uterine cavity; in the second, the ovary is implanted on or within the uterine wall and projects to the free surface of the endometrium or makes contact with the interstitial portion of the tube.

In 1900, Dudley[1] reported no pregnancies in his 6 cases in which the ovary "attached to its own ligament was suspended in the uterine cavity and stitched to the mucous membrane, hanging like a polyp." Tuffier,[2] in 1924 reported on a series of 29 patients. After having dilated the uterus with tents for twelve hours prior to operation, he implanted within the uterine cavity, a portion or all of the ovary, attached to its pedicle. He incised the posterior wall of the uterus nearest the site of the ovary to be implanted and sutured the ovary so that one-third of it projected into the uterine cavity. He took particular care to remove the interstitial portion of the tube. There were no pregnancies in any of his 29 patients, but he stated that Raymond Petit[3] "has had one case with delivery of a live child at term, while Estes[4] in 27 cases reported 2 full term living children and two miscarriages at three and four months."

Neither Estes nor Petit used the technique of Tuffier. Their implants were made at the cornu of the uterus. The first operation in 1900 of Petit[3] was followed by a normal pregnancy with delivery at term. He states that "we remained true to our original incision on the uterine horn." The work of both Estes and Petit illustrates the second type of implantation in which the ovary does not extend into the cavity of the uterus. Serdukoff[5] and Storer[6] used this second class of implantation without results except in one of Storer's patients who aborted.

Foster[7] used free ovarian grafts which extended within the uterine cavity but did not report pregnancies. Cullen, Watkins and Unterburger[8] are among those who made tubal implants into the uterus. Cullen[9] reported a normal full term delivery after the right tube and ovary had been removed and the outer half of the left tube sutured into the uterine cornu.

Little work has been done on animals using ovarian implants attached to the neurovascular pedicle. Uffreduzzi[10] concluded from his experiments on rabbits and guinea pigs that "with implantations of an ovary, or piece of ovary, into the uterine cornu, pregnancy cannot occur." Monson[11] obtained no pregnancies in 6 rabbits. He said that in the one animal

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in which the ovary survived intrauterine implantation, "it was in a state of delayed activity as evidenced by the absence of Graffian follicles." Lissiansky[12] noted that pedunculated intrauterine ovarian transplants in dogs became fixed and retained their vitality for a long period. Rychinski[13] conducted similar experiments on rabbits. Mairano and Placeo[14] concluded from extensive experiments on guinea pigs that the uterine cavity is a suitable environment for ovarian implantation. Ovaries implanted by them within the cavity of the uterus continued to function but no pregnancies occurred in any of their animals. A fairly extensive survey of the literature failed to reveal any instance in women or animals in which an *intrauterine* implant of an ovary was followed by pregnancy. *Uterine* implants of the ovary in women have made pregnancy possible occasionally.

The rabbit was chosen for my experimental work mainly because of its fecundity. If the reproductive life of the female rabbit is three years and of women thirty years, six months of observation on the rabbit is proportional to five years on women. Five years is a reasonable time in which to judge sterility in women under given conditions and six months should suffice for observing rabbits in these experiments.

I used the implantations of a part or all the ovary within the cavity of the uterus with preservation of its blood and nerve supply, and with distruction of the tubal connections between the uterine and abdominal cavities.

### EXPERIMENT 1. PARTIAL UNICORNATE UTERUS CONSTRUCTED FROM A BICORNATE ONE

Two does, six months old, neither or which had borne litters, were used. The abdominal field was shaved and strict aseptic technique was observed. Under ether anesthesia, the lower part of the abdomen was opened through a midline incision and the right ovary mobilized by dividing the outer leaf of the ovarian ligament. The left ovary and both fallopian tubes were excised and the ends of the uterine cornua were closed by linen ligatures. A longitudinal incision 4 cm. long was made through the median aspect of both cornua near their bases and the posterior cut margins of the two were sutured together with fine silk. The two anterior margins were sutured in like manner except at the upper 1 cm. through which was introduced the mobilized right ovary. The ovarian pedicle was sutured with fine silk to the cut anterior margins of the newly constructed unicornate uterus so that the ovary was retained well within its cavity. The two does were observed for four months, during which time they were placed repeatedly with a buck. At no time were any signs of sexual activity evidenced. At autopsy, no ovarian tissue remained in either rabbit and there were many adhesions about the implantation site. The uteri were pale, cylindrical, elongated and flaccid as those described by Fränkel[15] in the rabbit and by Hartman[16] in the opossum, after complete oophorectomy. Because of technical difficulties this type of operation was discontinued.

### EXPERIMENT 2. IMPLANTATIONS OF OVARIES AT THE END OF THE UTERINE CORNU

Two does, sixteen months old, each having raised litters, were operated on with the following changes from the previous procedure. To minimize trauma to the viscera, an oblique incision through the abdominal wall was made directly over the ovary. About 1 cm. of the distal end of the uterine cornu with the fallopian tube was excised. The ovary, without being mobilized, was drawn into the divided end of the cornu and sutured well within its lumen (Fig. 1). The severed end of the uterine cornu was closed by suturing its margins in part to one another and in part to the ovarian pedicle, in order to retain the ovary within the lumen.

To prevent the motility or contractions observed in rabbit uteri causing extrusion of the ovary as a foreign body, that portion

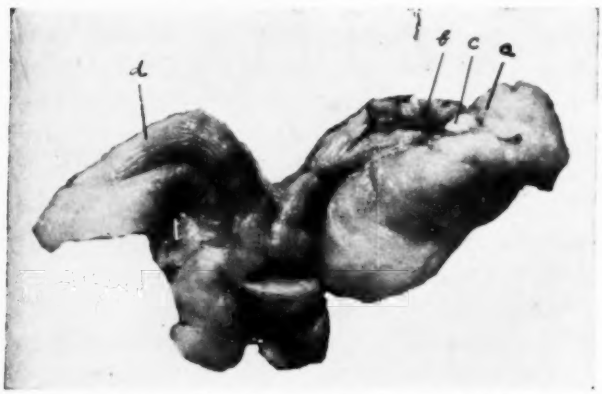


Fig. 1. Photograph of ovary implanted within lumen of uterine cornu; *a*, ovarian pedicle adherent to broad ligament; *b*, opened cornu, exposing part of *c*, implanted ovary; *d*, unopened cornu.

of the cornu containing the implanted ovary was fixed by suturing it to the base of the broad ligament. The abdomen was closed in layers with interrupted linen suture. In one rabbit both ovaries were implanted, in the other only one, the opposite one being excised. These rabbits were not bred and were autopsied two weeks after operation. All of each ovary had remained well within the cavity in which it had been implanted and appeared grossly normal. Microscopic examination disclosed apparently normal ovarian stroma in which were many primordial and growing follicles (Fig. 2).

This experiment proved that the implanted ovaries persisted and that this operation, as compared with that of Experiment 1, was technically much simpler and it therefore was adopted for Experiment 3.

### Experiment 3. Ovulation Stimulated in Implanted Ovaries by Normal and Artificial Means

Nine rabbits, nine to eighteen months old and each having raised one or more litters, were operated on by the technique described in Experiment 2. In 6 rabbits both ovaries were implanted, in 3 only one, the other being excised. Beginning one month after operation, the rabbits were placed frequently with a buck. All except two evidenced sexual activity by mating repeatedly and by vaginal signs of estrus, and four of them by nesting frequently. The failure of the two to show sexual activity may have been due to severe injuries from fighting. No litters were produced by any of the rabbits but it was reasoned that pregnancies might have been aborted or fetuses absorbed due to pressure on the ovaries, hence two of them were subjected to exploratory laparotomy two weeks after observed copulation. These two had had bilateral implantations and both had demonstrated pronounced sexual activity. The operations disclosed no pregnancy. One ovary was atrophied, due evidently ta constriction of the vessels in the pedicle. The other three ovaries were of normal size and were situated well within the lumen of the uterus. The uteri were grossly normal, the lumen of all cornua being patent to the site of implantation.

Desiring to increase ovulation and thereby to increase the possibility of pregnancy, 3 rabbits in this experiment were given intravenous injections of 10 c.c. of urine from women in their ninth month of pregnancy. They were placed with a buck after twenty-four hours and several times thereafter at three day intervals. Each time they accepted him, indicating, according to Patton, [17] that they were not pregnant.

At the end of six weeks, these three rabbits and one other of the 9 were given injections of urine from women in the late stage of pregnancy as Friedman[18] had noted in rabbits, that "one intravenous injection of 10 c.c. of urine from a pregnant woman causes ovulation." Ovulation is indicated by the presence of corpora lutea. The 4 rabbits were killed twelve hours after receiving a second injection of urine. All 9 rabbits in this experiment were placed with a buck three to ten days before being killed. Thus 5 were given natural

and 4 both natural and artificial stimuli for ovulation.

TABLE 1

SUMMARY OF AUTOPSY FINDINGS IN 18 RABBITS

| | | |
|---|---|---|
| A. | Total number of implants | 30 |
| B. | Average age of implants in months | 5 |
| C. | Condition of ovaries | |
| | (a) Ovaries communicating with lumen of uterus | 22(73.3 per cent) |
| | 1. One-fourth of surface | 6(20.0 per cent) |
| | 2. One-half of surface | 7(23.3 per cent) |
| | 3. Three-fourths of surface | 9(30.0 per cent) |
| | (b) Ovaries not communicating with lumen of the uterus and normal except for adhesions around them | 4(13.3 per cent) |
| | (c) Ovaries entirely atrophied or extruded from the animal | 4(13.3 per cent) |
| | (d) Rabbits in which one or both ovaries had corpora lutea and growing follicles | 12(66.6 per cent) |
| | (e) Rabbits in which only growing follicles were found | 4(22.2 per cent) |
| D. | Patency of uterine cornu | |
| | (a) Lumen patent to site of implant | 30(100.0 per cent) |
| E. | Number of rabbits presenting adhesions | 8(44.4 per cent) |
| | (a) Involving both cornua | 2(11.1 per cent) |
| | 1. Many adhesions | 1(5.5 per cent) |
| | 2. Few adhesions | 1(5.5 per cent) |
| | (b) Involving only one cornu | 6(33.3 per cent) |
| | 1. Many adhesions | 0 |
| | 2. Few adhesions | 6(33.3 per cent) |

Autopsy of the 9 rabbits performed five to eight months after implantation revealed no pregnanies. All uteri appeared grossly normal except for a few unilateral adhesions in 4 (Table 1). In none of the rabbits was there a connection between the cavity of the uterus and abdomen.The lumen of all uteri was patent and it was mechanically possible for fertilization to occur. One ovary was atrophied in each of 2 rabbits with bilateral implantations. Each of 2 other rabbits with bilateral implantations had one ovary outside the uterine cavity (13 per cent).

Ovaries were considered functionally normal when they conformed to the following criteria: (1) grossly normal ovarian tissue free within the lumen of the uterine cavity; (2) microscopically normal appearing ovarian stroma in which primordial follicles, growing follicles and corpora lutea were present (Figs. 2 and 3). Ova were demonstrated microscopically in the washings from one uterus containing a functionally normal implant according to this criteria. Since the uterus had no connection with the abdominal cavity, ova found within could be there only as the result of ovulation from the implanted ovary. Each of the rabbits had one or more functionally normal intrauterine ovaries containing many corpora hemorrhagica and corpora lutea. Serial sections of them failed to reveal ova retained with corpora lutea and only occasionally within corpora hemorrhagica. Therefore ova from many luteinized follicles must have been extruded directly into the uterine cavity.

### EXPERIMENT 4. PORTION OF OVARY IMPLANTED

Two rabbits, their ages and pregnancy records similar to those in the previous experiment, were operated on in like manner except that one-half of each ovary was resected longitudinally in an effort to obtain less crowding of the implant and to simulate human implants in which a diseased portion of the ovary is excised. Furthermore, the uterine cornu at the site of implantation was not fixed to the base of the broad ligament.

After one month they were placed repeatedly with the buck. Six months after operation and seven days after observed copulation the rabbits were killed. At autopsy the uteri were nonpregnant and grossly normal. One ovarian implant had atrophied, the others remained attached within the uterine cavities by broad scar tissue bases and were functionally normal according to the foregoing criteria.

### EXPERIMENT 5. OVARIES IMPLANTED WITHIN PREGNANT UTERI

With the idea of making operation easier, bilateral implantation of the entire ovary was done on 3 rabbits one to two weeks pregnant, using the technique of Experiment 4. In two uteri all fetuses were removed; in the other only the distal portion of each cornu sufficient for the

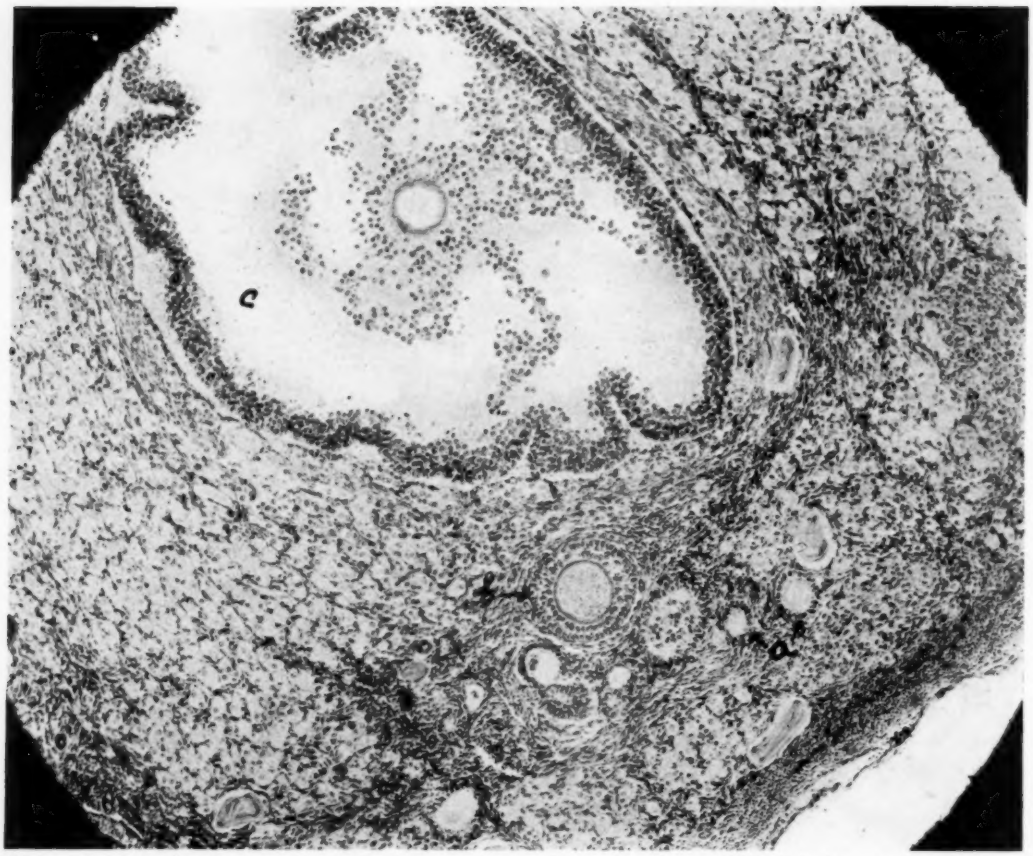


FIG. 2. Photomicrograph of normal ovarian stroma containing: *a*, primordial follicles; *b*, developing follicle; *c*, Graafian follicle.

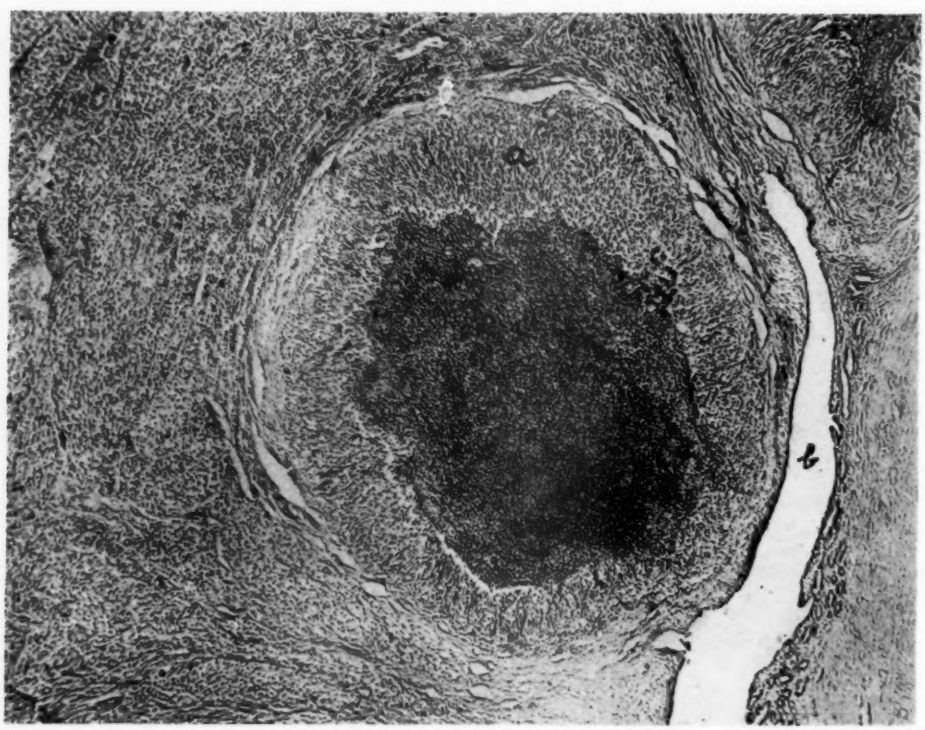


FIG. 3. Transection of early corpus luteum from implanted ovary in a rabbit. Corpus luteum (*a*) bulges into uterine cavity (*b*).

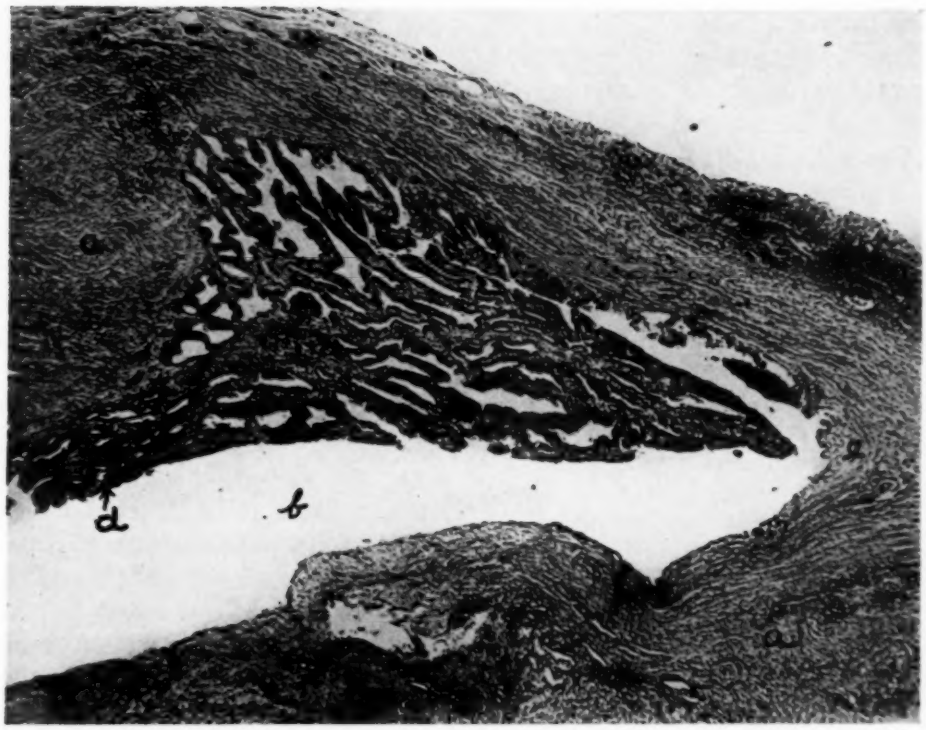


FIG. 4. Photomicrograph showing fibrous connective tissue union of ovarian implant to amputated end of uterine cornu; *a*, ovarian tissue; *b*, uterine cavity; *c*, wall of uterine cornu; *d*, endometrium; *e*, scar tissue.

FIG. 5. Transition from columnar epithelium cells of endometrium to cuboidal cells of germinal epithelium of ovary. *a*, ovarian tissue; *b*, uterine cavity; *c*, union between ovary and uterus; *e*, epithelium of ovary; *f*, epithelium of endometrium.

implant was evacuated; but the remaining fetuses did not go to term. Attempts at breeding were made as in the previous experiment but at no time were they observed to accept the buck. Rabbit No. 10 was given injections of urine and killed twelve hours after receiving the second injection as in Experiment 3. Four to seven months after operation and three to ten days after having been placed with a buck, the other rabbits were autopsied. Except for many adhesions the uteri were grossly normal. In 2 of the animals one ovary was outside the uterine cavity. Each rabbit, however, had at least one ovary which had remained within the uterine cavity and which appeared functionally normal. Endometrium overgrew part of one ovary of rabbit No. 10 as will be noted below under healing of the implants.

Failure to fix the site of implant in the 5 rabbits used in Experiments 4 and 5 resulted in 20 per cent of the ovaries being found outside the uterus as compared with 12 per cent in Experiment 3 in which the site of implantation was fixed to the base of the broad ligament.

### MODE OF HEALING OF THE IMPLANT WITHIN THE UTERUS

Scar tissue union between the uterus and the base of the implant was present in every instance. Microscopically, atrophy of the endometrium with its replacement by fibrous connective tissue was often seen in those places where at operation endometrium had intervened between the uterine cornu and the attachment of the ovarian pedicle.

The endometrium proliferated or underwent metaplasia only in rabbit No. 10. Part of the surface of one of its ovaries was pink and velvety and at the angle made by the ovary joining the endometrium were short polypoid projections or folds similar grossly to endometrium. Microscopically the epithelium of the endometrium was continuous with the germinal epithelium of the ovary (Figs. 4 and 5). There was a gradual transition from the high columnar cells of the endometrium to low columnar, and then to the cuboidal cells of the germinal epithelium covering the ovary. The endometrial epithelium had undergone proliferation and metaplasia to become similar to and continuous with the germinal epithelial cells of the ovary.No endometrial implants were seen within any of the ovaries.

### SUMMARY

In a total of 18 rabbits in which intrauterine implantation was done, one or both ovaries persisted in the cavity of the uterus in all except 2. In the 16 rabbits in which one or both ovaries persisted, the lumen of the uterus in all was patent to the implantation site so that ovulation directly into the uterine cavity was possible. In 12 of these rabbits, functionally normal ovarian tissue was demonstrated microscopically. The presence of corpora lutea indicated recent ovulation and ova were found within the cavity of the uterus. In spite of frequent copulation no pregnancy resulted.

The base of the implanted ovary always united to the uterus by fibrous connective tissue but union between the epithelium covering the ovary and that lining the uterus was noted in one implant.

### COMMENT

Failure to obtain pregnancy after intrauterine implantation of the ovary in rabbits may be due to expulsion of the ovum from the uterus soon after ovulation. Ova may not be readily susceptible to fertilization and implantation immediately after ovulation so that follicular fluid escaping with them into the uterine cavity may result in excessive contractions of the uterus sufficient to expel them. If fertilization normally occurs within the fallopian tube, the lumen of which is exceedingly small compared to that of the uterus, the greater surface area within the uterus may render contact between sperm and ova unlikely. The implants may act like uterine polyps in preventing pregnancy.

This experimental work and operations upon women, indicate that implants *within the cavity of the uterus* offer little hope for pregnancy. Literature, however, reveals an occasional pregnancy with implants merely communicating with the cavity of the uterus.

## CONCLUSIONS

1. In rabbits two weeks to eight months after intrauterine implantation of ovaries with preservation of the neurovascular pedicle, grossly and microscopically normal ovarian tissue usually persisted.

2. After intrauterine implantation of ovaries of rabbits, ovulation occurred into the uterine cavity, behavioristic sexual activity continued but pregnancy did not result.

3. In women, uterine implants of the ovary, but not those extending into the uterine cavity, offer prospect for an occasional pregnancy.

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# NEW INSTRUMENTS

## A NEW BLOOD TRANSFUSION NEEDLE*

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THERE is no other step in the technical procedure of indirect unmodified blood transfusion that is more important or more difficult than the proper performance of the introduction of the needles into the veins of recipient and donor. This particular procedure alone accounts for the greatest number of unsuccessful transfusions of unmodified blood and has been due in great measure to the type of needle used. The needle here to be described is presented with the belief that some of the difficulties and objections of the needles heretofore in use are obviated and venipuncture can be more easily, more safely, and more rapidly performed.

### DESCRIPTION

The needle consists of a cannula (Fig. 1 a) and an obturator (Fig. 1 e). The cannula possesses a square hub having corrugated surfaces and provided with a small slot into which is fitted a projection of corresponding size on the obturator (Fig. 1 h) for the purpose of locking the obturator in the cannula. The point of the cannula tapers to a round, dull edge, as shown in the enlarged longitudinal section (Fig. 1 c). The wall of the cannula is thin so as to provide a sufficiently large lumen and yet permit the external diameter to be relatively small. The inside surface is made

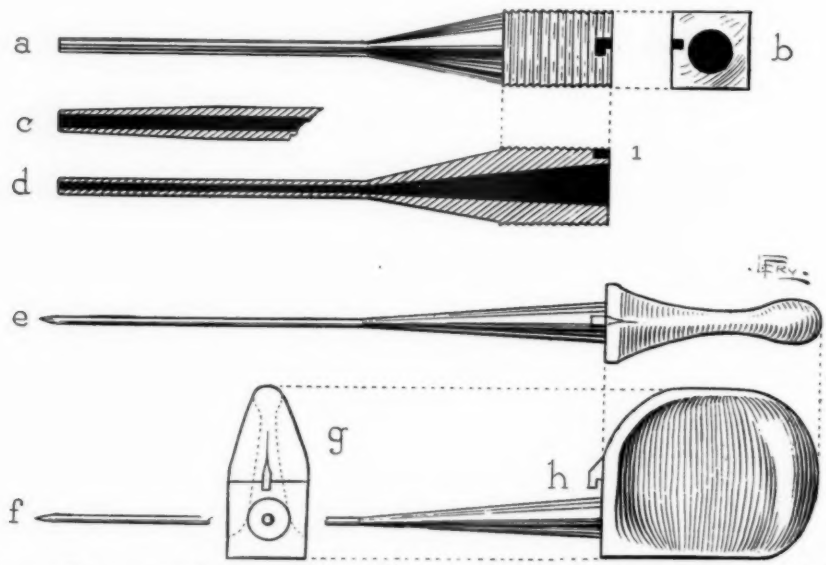


FIG. 1. Transfusion needle: a, cannula; b, end view of hub; c, enlarged longitudinal section of tip of cannula; e, obturator, upper view; f, obturator, side view.

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of hyperchrome steel and the outside surface is nicheloid.

The obturator possesses a sharp cutting point which projects just beyond the cannula when the obturator is fitted into the latter. The obturator also has a handle with two concave corrugated surfaces of sufficient width and breadth to allow a firm grasp with the thumb and finger (Fig. 3).

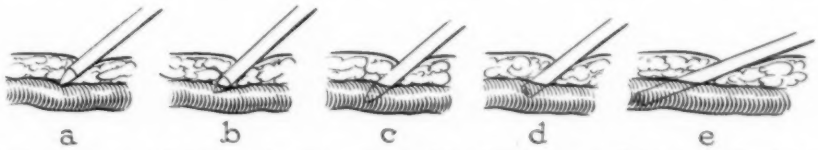


Fig. 2. Diagrammatic representation of venipuncture: a and b, piercing superficial wall of vein; c, needle in lumen of vein; d, obturator retracted leaving blunt end cannula; e, inserting cannula farther into vein.

### TECHNIQUE

A small wheal is produced immediately over the vein by the intracutaneous injection of 0.5 per cent novocaine. The venipuncture is then performed in two steps: (1) piercing the skin, and (2) inserting into the vein. This is facilitated by retracting the skin immediately over the vein to one side (as shown by the thumb of the left hand in Fig. 3), then piercing the skin. This precaution obviates the possibility of simultaneously piercing the vein as a result of the exertion of too great force on the needle. Once through the skin, tension is released, allowing the skin with the needle in it to return to its original place immediately over the vein. Then with the handle of the obturator, the operator simply guides the cannula into the vein by piercing its superficial wall. Once it is in this position the obturator is retracted, and the blunt end cannula can then be inserted farther into the vein without fear of nicking or piercing the wall at any other site (Fig. 2).

### ADVANTAGES

1. The needle is made of a rustless, stainless material with a smooth, highly polished inner surface.

2. The lumen is sufficiently large to provide a free flow of blood, but possesses a relatively small external diameter so as to facilitate venipuncture when small veins are encountered.

3. The likelihood of producing a hematoma or injuring the vein is greatly diminished, because after retracting the sharpened obturator it is a blunt end cannula that is inserted farther into the vein.

Fig. 3. Method of venipuncture by first piercing skin over vein after this has been pulled to one side by left thumb.

4. Venipuncture is considerably facilitated by guiding a cannula into a vein with a sharp pointed obturator provided with a large handle permitting firm purchase and resultant ease in manipulation.

# A MODIFIED NEEDLE HOLDER

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OMAHA, NEB.

IN using a needle holder of the Mayo Hegar type it is usually necessary to remove the finger and thumb from the rings and run the hand down the holder, thus shortening the grip, at the time the needle is being passed through the tissues. If the thumb and finger are kept in the rings of the holder, the rotation of the holder required to insert the needle becomes rather awkward to perform. There are two methods in common use which make the maneuver of running the hand down the holder somewhat easier. Some surgeons find that if the fourth finger and thumb are used in manipulating the holder, it is necessary to remove only the thumb in order to get the hand fairly well down on the holder. In rotating the holder with the usual semicircular needle, however, as long as the fourth finger is in the ring, extremes of rotation become difficult. Other surgeons insert only the thumb in one ring of the holder and hold the other ring in the grasp of the third, fourth, and fifth fingers. If the thumb is not passed very far into the ring this method is fairly satisfactory. It is necessary to remove only the thumb and since the fingers are not passed through the other ring it is relatively easy to shorten the grip on the holder and rotate it. Many times, however, especially if the thumb is passed well into the ring, the removal of the thumb necessitates a definite maneuver and slows up the work.

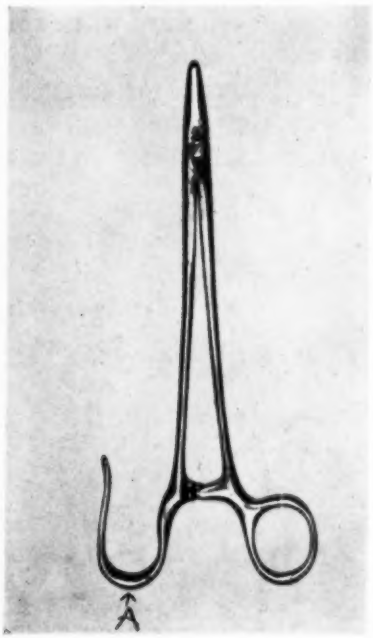


FIG. 1.

We have modified an 8 inch Mayo Hegar needle holder by opening up one ring as shown in the illustration and have found that the use of the holder is considerably facilitated. The open ring is used for the thumb and the edge of the ring at A has been beveled and widened by braising on additional metal so as to fit the side of the thumb, where pressure is made in opening the holder. In using this modified needle holder either of the two methods described may be used. The thumb is inserted or removed from its ring by the mere motion of the hand up or down the holder.

# PORTABLE APPARATUS FOR HYPEREXTENSION OF THE SPINE

WALTER E. JOHNSTON, M.D.

VICKSBURG, MISS.

THERE are many simple and effective methods used in the reduction of crushed fractures and dislocations of the spine. In some cases, however, it is difficult to maintain the desired degree of hyperextension with safety and comfort to the patient while applying a snug plaster jacket.

The apparatus described here has been used with gratifying results in several cases. All these patients remained perfectly relaxed and comfortable throughout the entire operation of reduction and application of plaster. The hyperextension was done slowly, which made it possible to examine the patient at frequent intervals.

The apparatus is made somewhat on the principle of the Goldthwait irons, but has the advantage of being adjustable for each individual case (Fig. 1). It consists, principally, of two upright T's, one fixed firmly to the base, the other made to slide by the use of a screw. On each upright piece, there is a rocker-arm which is held in place by a removable pin. Various sized spring steel bars may be inserted into the slot of each rocker-arm. By forcing the two ends toward each other with the screw, the bars are sprung into an arc of any degree. The apparatus weighs only 8 pounds, but will support, with ease, several hundred pounds. The frame may be placed on any table or bed.

After bars of the proper length have been chosen and placed in the slots, the screw is given a few turns to lock them in place. A heavy piece of felt is then placed over the bars and the patient lifted into position (Fig. 2). The screw is given an occasional turn until the desired amount of hyperextension is obtained.

Extreme hyperextension may be accomplished with ease and very little discomfort to the patient (Fig. 3). The desired position may then be maintained while a snug plaster jacket is applied.

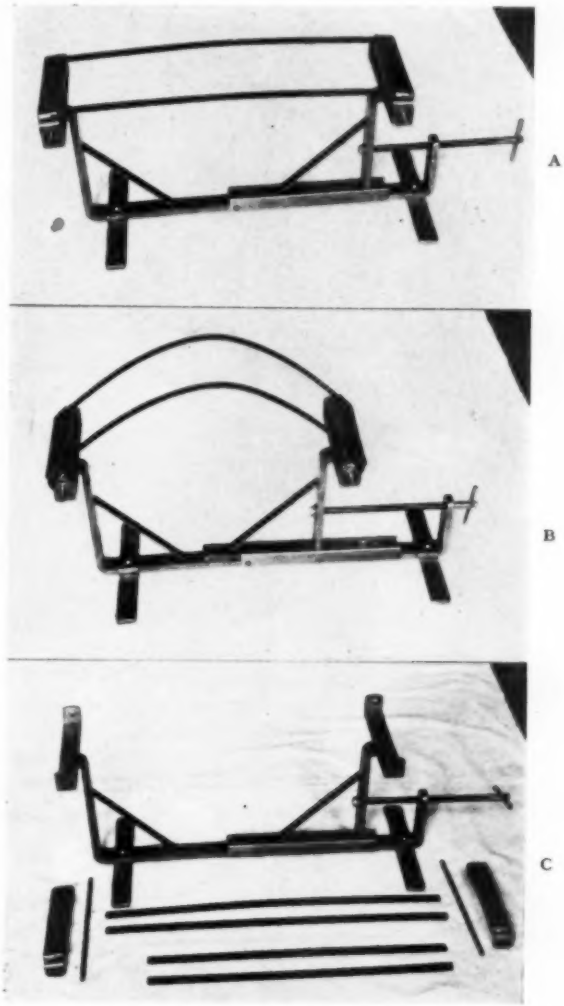


FIG. 1. A. Frame as it appears before tension is made on screw. B. As tension is made on screw, bars are forced into an arc. C. By removing pins at each end, rocker-arms and bars fall apart. Two lengths of bars are shown here, made of spring steel, $\frac{1}{8}'' \times \frac{1}{2}'' \times 14''$ and $\frac{1}{8}'' \times \frac{1}{2}'' \times 18''$.

After the plaster has been applied, the patient should remain on the frame until the plaster is firmly set (Fig. 4). The frame is removed simply by releasing tension on the screw and removing the pin in one or both of the rocker-arms. The bars are then easily withdrawn from under the cast.

Roentgenograms of one patient's spine, taken before and after reduction on this frame, are illustrated (Fig. 5).

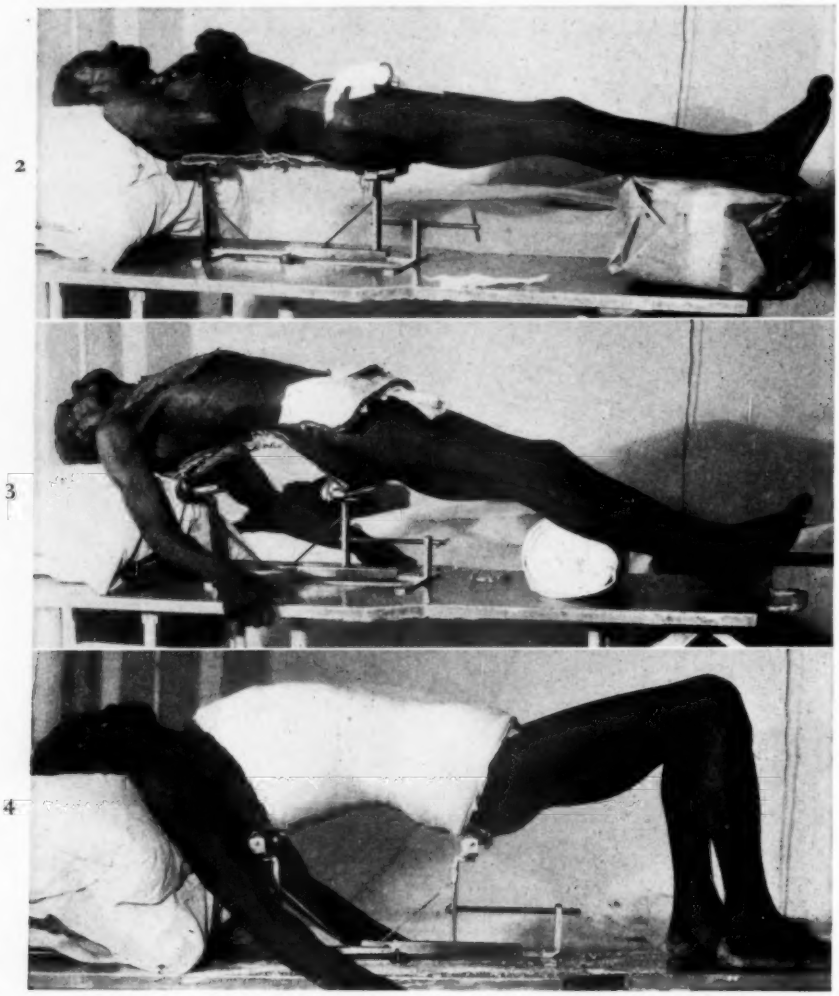

FIG. 2. Apparatus can be used on any table. Felt is placed between patient and bars. Patient is made as comfortable as possible before hyperextension is begun.

FIG. 3. By slowly turning screw, hyperextension can be accomplished with ease. Patient is in an excellent position for frequent examination, including *x*-rays.

FIG. 4. Bars have been incorporated in padding and plaster. Patient is allowed to remain in this position until plaster sets, after which, apparatus is taken apart and bars withdrawn.

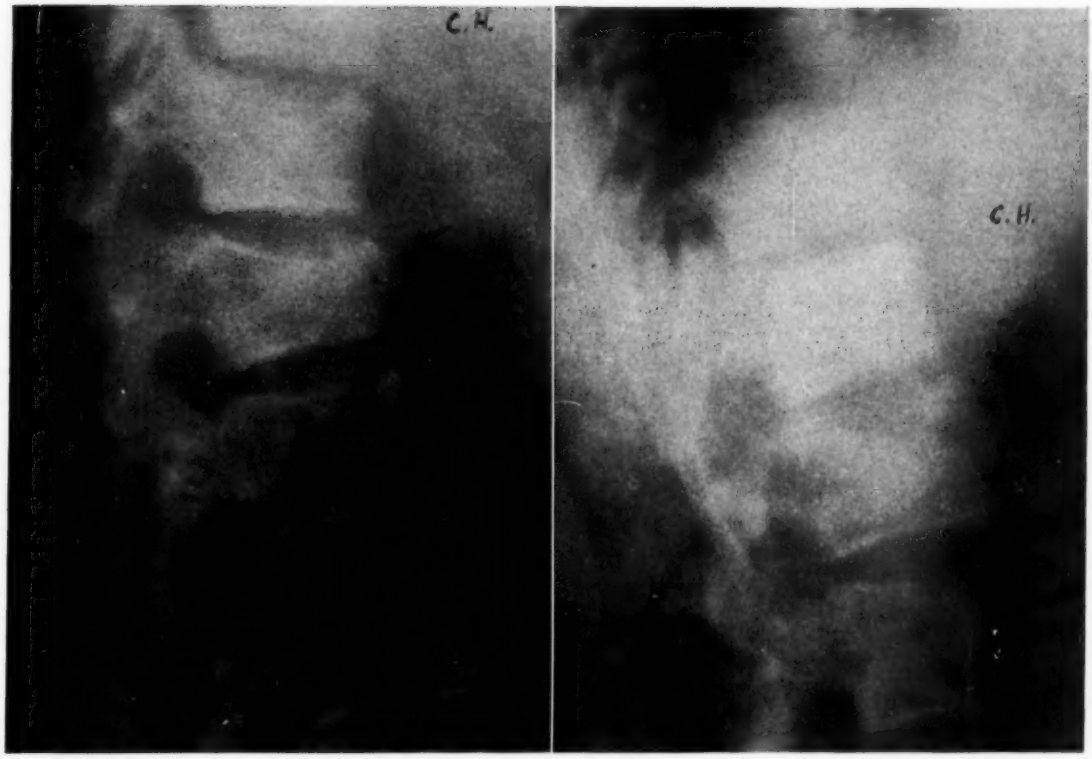


FIG. 5. Roentgenograms of crushed fracture of first lumbar vertebra, before and after reduction.

# JOSEPH LEIDY

CALLED "the greatest naturalist this or perhaps any country ever produced," Joseph Leidy was born in Philadelphia on September 9, 1823. He came of a family that fought in the American Revolution, a grandfather having served under Washington at Valley Forge and at Yorktown.

Young Leidy, at the age of ten years, was sent to the Classical Academy under the Reverend William Mann. He was an indifferent student. He was only interested in tramping the country, drawing, and studying all sorts of queer insects and worms. Leidy himself said, "I was always . . . called a 'queer boy,' . . . anxious to see how plants and animals were made."

When sixteen, he worked in the apothecary shop of his cousin, Dr. Napoleon B. Leidy.

He began the study of medicine at the University of Pennsylvania in 1840, and graduated in 1844. Paul B. Goddard gave Leidy instruction in the use of the microscope in 1841. This sowed the seed for some of the most brilliant research of all time. His graduation thesis was, "The Comparative Anatomy of the Eye of Vertebrated Animals."

Leidy became Goddard's assistant (in anatomy) and prosector to Professor Horner. In 1845 he began private practice for which he was ill fitted, and of which he did not make a success. In 1853 he succeeded to the chair of Anatomy at Pennsylvania, and held it for thirty-eight years. He taught anatomy as a pure science. He was a firm believer in evolution and a strong adherent of Darwin.

Notwithstanding his duties at the University, he also filled the chair of natural history at Swarthmore (1871–1881). With the development of the department of zoology at Pennsylvania, he was made professor of that department. On July 27, 1885 he was made president of the Faculty and Professor of Biology in the Wagner Institute of Science.

In 1869, Franklin and Marshall College, and in 1886, Harvard, gave him the honorary degree of LL.D.

In 1865 he married Anna Harden of Kentucky. They had no children but adopted a daughter.

We have not the space to record his writings. In 1851 he published the first account of the successful transplantation of tumors. Once while eating some pork he noticed some black specks in it. This led to the discovery of the method of entrance of trichina to the human being. His work on parasites brought him world renown.

Throughout his life he was a member of and contributed to the scientific discussions of the Philadelphia Academy of Natural Sciences.

His name is engraved on the cornice of the Zoological Building at the University of Pennsylvania. In the border of the Ashurst Reading Room at the College of Physicians his name is between those of Virchow and Hippocrates. His statue stands in City Hall Plaza, Philadelphia.

Leidy was an intellectual giant, a man famous in more than one field. We are told he had no enemies. He cared not for wealth. He was laden with high honors.

He died on April 30, 1891.

T. S. W.

[From Fernelius' Universa Medicina, Geneva, 1679.]

# BOOKSHELF BROWSING

## "PLAIN REMARKS"— AMERICA'S FIRST MANUAL OF SURGERY*

WILLIAM M. MILLAR, M.D.

CINCINNATI, O.

THE modern system of medical education stands in strong contrast with the conditions that existed in North America at the time of the Revolution. To be sure, the training offered during the eighteenth century everywhere was meager and insufficient but the American provinces in general were much worse off in this respect than was the mother country. There were but two permanent hospitals in the thirteen colonies. New Jersey alone had organized a "state society." There were no medical journals and the first *Medical Quarterly* was not to appear until 1787. Furthermore, the actual training received by the great majority of doctors was for the most part wretched. Only a few were fortunate enough to have had their schooling in the large Continental and British clinics before they emigrated or because they had returned to Europe for that purpose. While it is true that there were two small medical colleges, one in Philadelphia and the other in New York City, the actual number of graduates that were turned out of these institutions were comparatively few. The few textbooks used throughout the land were written by French and English authors and these volumes were few in number and quite expensive. The average man who wished to enter the profession was obliged to learn his medicine from an older man and learned by working and helping him. All in all, conditions were wretched. But in 1776 the first manual of surgery to be written and printed in America was published in a patriotic attempt to improve these matters. It was intensely practical and was especially composed to help the young regimental surgeons and surgeons-mates of the newly organized colonial armies.

Every reader of American history recalls John Paul Jones, the sailor, ex-pirate, and victor of Flamborough Head, but very few have ever heard of his contemporary, John Jones, the scholar and surgeon, although in his day he was well known to the medical profession on both sides of the Atlantic. One of the best educated men of the period, he was the doctor of Franklin

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and Washington, a lithotomist of international reputation, and with Samuel Bard was a founder of the medical school of King's College (later Columbia). Here he served as the first professor of surgery. But his most important contribution, which has now been almost completely forgotten, was his concise, thin, well-written manual of surgery.

Jones had a magnificent background and a superb training for a doctor. With a great grandfather, a grandfather, and a father who were physicians, a descendent of a family who had come to Pennsylvania in 1682 and settled in the famous Quaker village of Merion, he was well ballasted with tradition. But his father was not content with this. When a son who had been born in Jamaica, Long Island, in 1729 stated that he wished to follow the same profession, it was seen that he was given the best possible training. Privately educated until the age of eighteen, the lad was then placed in the home of Doctor Thomas Cadwalader[1] in Philadelphia, and with him commenced the study of medicine. The ground work laid, the young man was sent to London to attend the lectures of Hunter, MacKenzie, and Percivall Pott. Next the American proceeded to France and earned a degree in medicine at the University of Rheims. Not content with this, he visited the clinics of LeCat and LeDran at the Hotel Dieu. Time was spent in Leyden which the late Boerhaave had made so famous, and finally his European studies were terminated in Edinburgh where it will be recalled Monro *primus* was then at his peak. At last the young Colonial returned to America and began to practice. The extremely well-trained youngster almost immediately won recognition. He was an excellent accoucheur and it is said that the young Provincial performed the first lithotomy in New York. Mitchell states that the average time for this operation was only ninety seconds!

Jones interrupted his practice and took part in the French and Indian War under Sir William Johnson in the Lake George country. Little is known of his adventures, but there is a record existing today which states that in 1758 a wounded, captured French general was placed under his care and nursed back to health.

About this time the young surgeon was taken sick with what appears to have been a pollen asthma. A sea voyage was prescribed and he returned to London. Friendships were renewed and he became quite well acquainted with Percivall Pott. The illness improved greatly with this change and he was able to return home. Since the American had been abroad, the political aspect of his country had changed materially. Discontent was rife throughout the provinces and war was imminent. The Colonies were remarkably poorly prepared in every way but nothing was worse than their militia medical service. As was stated previously, it was in a definite attempt to counteract these conditions that Jones wrote his book. The full title of the work was "Plain, Concise, Practical Remarks on the Treatment of Wounds and Fractures," and the monograph was combined with a book of van Swieten's: "The Diseases Incident to Armies with Method of Cure," a work by John Ranby, the Surgeon General of the British Army, and a treatise on scurvy by William Northcote, "Many Years in the Sea Service." This book was Jones's only written work. When he was still in New York he spent a number of years preparing a monograph on meteorological observations of that region. Just as the manuscript was complete, however, and ready for the publisher it was destroyed, it was thought, by a fellow professor "who had perfidiously seized upon it." So disgusted was Jones by this catastrophe, he vowed that he would never write again.

[1] Cadwalader, a really prominent man had been a pupil of Cheselden and as early as 1730 had given a series of practical anatomy demonstrations. He is best remembered for his essay on the West Indies Dry Gripes.

The war continued and when the British ultimately captured New York Jones moved to Pennsylvania where he had many friends. It is interesting to note that the British offered him personal protection and immunity if he would return but he refused all offers of pardon. As his asthma was somewhat improved by the change of climate he decided to make Philadelphia his permanent home when that city was finally evacuated by the enemy. In his new location the former New Yorker soon became prominent in both a social and a professional way. He was a member of the Philosophical Society and shortly was named as its curator. After a time he was appointed to the staff of the Pennsylvania Hospital. He became a warm friend of Franklin with whom he had many things in common. Indeed he operated upon the famous statesman for stone, was present at his last illness, and was remembered by him in his will.

In 1790 while in New York City Washington became sick. Jones was sent for, arrived on the fourth day of the disease, found and treated the condition which resulted from "an inflammatory nature terminating in a state of debility." A few hours afterward the President was greatly improved and shortly afterward was quite well. For this reason it is not strange that when the Capitol was moved to Philadelphia Jones became an intimate friend as well as the private physician of Washington. In fact, his last social visit was to the President's home. On his return a sudden change of weather met him, a chill followed, and he was forced to bed. Diarrhea, fever and cardiorespiratory complications followed rapidly and in less than a week he was dead. The exact date was June 23, 1791.

The rather lengthy dedication and introduction to "Plain Remarks" does not begin to approach the preface of Richard Wiseman's "Treatises" but nevertheless certain parts are excellent. It is true that they are written in the labored buckram style of the time but they escape ridicule by their obvious sincerity and by the belief that the man was a true patriot who desired to help and aid his country. A few parts are worth citing:

*Introduction:*

"To Doctor Thomas Cadwalader,
Physician in Philadelphia;
Sir,

While speculative philosophers are disputing about the origin of evil and foundation of morals; and furious bigots, contending for different modes of faith, the practical good man will endeavor to employ himself in alleviating those evils which he finds incident to human nature without too vain and curious an inquiry into causes, the nature and operation of which lie far beyond the narrow limits of human understanding.

The present calamitous situation of this once happy country . . . demands the aid and assistance of every virtuous citizen: and though few men are possessed of those superior talents, which are requisite to heal such mighty evils as now threaten the whole body politic with ruin and desolation; yet every man has it in his power to contribute something towards so desirable an end, and if he cannot cure the fatal disease of his unfortunate country it will, at least, afford some consolation to have poured a little balm into her bleeding wounds.

Influenced by these motives, I have endeavored to select the sentiments of the best modern surgeons upon the treatment of those accidents, which are most likely to attend our present unnatural contest; and as many of the gentlemen engaged in that service are young men whose opportunities of instruction or practice, have been confined within narrow limits, I flatter myself that such of them, at least, as are conscious of their own defects, will find in the piece, no unuseful guide. . . .

A few excerpts from the "Introduction to the Students and Young Practitioners in Surgery throughout America" may be quoted:

. . . If any of you by observing the following rules should save the life, or even the limb of but one citizen, who has bravely exposed

himself in defense of his country, I shall think myself richly rewarded for my labour. . . .

A judicious surgeon will always find his powers and abilities of assisting the wretched proportionable to the time he has spent, and the pains he has bestowed, in acquiring the proper knowledge of his profession. . . .

To be proficient in an art which requires reiterated experiment; and when the whole subject is liable to such variation, not only requires a good deal of time, but much sagacity and judgment. . . .

[And] as to these gentlemen, who will neither read nor reason, but practise at a venture, and sport with the lives and limbs of their fellow creatures, I can only with Dr. Huxham, advise them seriously to peruse the sixth commandment, which is, "Thou shalt not kill."

The actual manual is divided into eleven chapters. With the experience of the first great World War still fresh in our minds they are amusing and interesting reading but the modern reader should not be too harsh and critical. The work makes no pretense of originality as the best Continental men are cited freely, and is truly a concise compend of the best surgical knowledge of the time. As Colonel Duncan has pointed out in his admirable book, "Medical Men in the American Revolution," Jones wrote before the time of vaccination (direct inoculation from contact, of course, had been used since Cotton Mather's time). There was no anesthesia and the stethoscope and clinical thermometer were still to be invented. It was an age of faith combined with a sturdy belief in the value of frequent venesections and a few strong medicines.

Chapter One deals with wounds in general and gives a description of the kinds and their courses. It is frankly taken from the classification of Boerhaave. Jones strongly favors a minimum of treatment and with Sharp recommends a dry soft lint for bandages and states an advantage of this dressing is its ability to check hemorrhage.

Chapter Two deals with inflammation. Chapter Three summarizes the various varieties of wounds which are divided into those that are incised, punctured, lacerated and contused. In general for the first condition he advises debridement and recommends that the wound be thoroughly cleansed, that all clotted blood and foreign bodies be removed, and the wound then closed loosely with needle and ligature. Limbs are to be flexed in cases with cut tendons and in lacerations as much skin as possible is to be saved. Contusions are to be opened when and wherever necessary.

Chapter Four: Penetrating Wounds of the Thorax and Abdomen. Intestines should be reduced and if the omentum has become black and gangrenous it should be ligated and the dead portion removed. The therapy of chest wounds is completely opposed to the course adopted in the American Civil War and other conflicts of the nineteenth century. The wound is to be opened and an external orifice made to procure a free discharge of blood. But with the abdomen watchful waiting is in order and operation is not to be considered.

Chapter Five: Of Simple Fractures of the Limbs. Violent extension should be shunned and a natural way of rest looked for and used. The young surgeon is warned to be on the lookout for pressure sores and especially for those on the heels of splinted legs. He is told to find the position of ease taken by the patient and to adapt the fracture to that. For example, one should flex the arm in treating a broken humerus, use a sling and strap the limb tightly by the side of the body. The patient with a fractured thigh should be placed on the side with the knee half bent to avoid muscle pulls which would tend to bring the fragments apart.

Chapter Six: On Compound Fractures. There are two schools: those who favor immediate amputation for almost any bad compound fracture and those who are opposed to this drastic procedure. The "Truth perhaps, may be somewhere between both and to hit the happy golden mean constitutes the perfection of human judgment." Jones shrewdly noticed that

Pott[2] whom he held to be a proponent of immediate amputation, lived in a large city and did most of his work in hospitals, and that others who advised waiting, among whom were Kirkland and Gooch, lived in the country and their practice there was for the most part with private cases. A great deal depended upon the "state of air." The young surgeon is told that a good working rule to follow is that in all fractures around the joints as well as those of the oblique variety which could not be held in place should be amputated. But if one was determined to wait, it is necessary to "Dilate the wounds first to free it from loose splinters and second for drainage." Then apply dry lint and apply a cast made from cerate. Scarifications are improper but counter-incisions for pus pockets must be made especially in the dependent portions of the leg. A compound fracture should be dressed at least once a day and oftener in hot weather. An oil cloth will help to keep the skin and the dressing clean, but at the first sign of gangrene amputate. Strangely enough, gas gangrene was not recognized as such even in the American Civil War (1861–65), but Jones gives us a classical description of it.

*Gas Gangrene:*

On the contrary, when a mortification takes place in consequence of a gangrenous disposition of the juices, whether the injury be more or less severe, the muscular and membranous parts are corroded by an acrid lymph, the membrane adipose is filled with air bubbles, producing an extensive emphysematous tumor in the skin which is not yet apparently diseased though it plainly points out the tragedy which is acting underneath; at this period a fever often accompanied with a delirium, great dejection of spirits, and particular wildness in the looks come on, the pulse is generally quick, low, fluttering, and unequal, according to the age and strength of the patient.

Incisions now made through the skin give pain, and its vessels discharge a florid blood, which proves that circulation is carried on, during the gangrenous state of the muscles and adipose membrane, which are of a yellowish brown colour, and soon change for the worse; the skin becomes greatly inflated, and when pierced, discharge from beneath, a quantity of frothy matter with air; at last the skin itself turns livid, and a general mortification closes the scene.[3]

The treatment prescribed was quinine and amputation.

Chapter Seven: On Amputation. A young surgeon should rehearse the operation "attentively in his own mind," choose his own assistants and avoid a "useless crowd of spectators." Then there follows detailed descriptions. Frozen fingers should be cut off, and a removal of cartilage which will promote speedier healing and granulation is advised on digital amputations.

It is of interest to note that Baron Larrey comments in his "Memoirs"[4] on the technique of the American army surgeons and contrasts them with his French confreres. Under the subject of amputation he declares that the colonial doctors operated much sooner and at the first sign of trouble, while the French, who were inclined to temporize, lost many more cases through their "watchful waiting" policy.

Chapter Eight: On Blows of the Head. Erysipelas of the scalp and careful observation of all puncture wounds are discussed.

Chapter Nine: Of Injuries Arising from Concussion or Commotion. Recommended anodynes are clysters and bleeding.

[2] As a matter of fact, Pott was not 100 per cent in favor of this rule. In his book on fractures he advised waiting on certain selected cases. Perhaps he still remembered the treatment of his own now historically famous ankle!

[3] One cannot help wondering whether Jones first knew and learned of this condition in Europe. It would seem likely that he did because Quesnay in 1745 gives Peyronnie credit for exact observations on the character of the disease. Fabricius Hildanus in his "Opera Omnia" (1746) mentions it, and so does De la Motte in 1771. On the other hand Thomas Kirkland (1786) and Pott (edition of 1790) who knew Jones and who were the first modern British surgeons to describe it, wrote their treatises after the Manual was published.

[4] Memoirs de Chirurgie Militaire et Campagnes. Paris, J. Smith, 1812, Tome 2, p. 492.

Chapter Ten: Of Injuries Arising from a Fracture of the Skull. Trepanning is discussed and is in order, first to relieve complaints; second, to give a discharge to matter from inflammation of the dura mater; third, as a prevention for further trouble.

Instructions for the elevation of depressed skull fractures: If there is a depression remove the entire piece. "A troublesome fungus" may arise "in the course of the cure but if a sponge be placed on it, the granulation will grow into the sponge and render removal easier . . . "

Chapter Eleven: Of Gunshot Wounds. Remove the bullet, check hemorrhage, and if possible, ligate the injured vessels. Ranby and LeDran advise as little probing as possible or the use of forceps as all such irritations only increase the consequent pain and inflammation. Dressings should be "light" and "easy." If necessary use milk and bread poultices. Bleed, clyster, perspire and avoid everything hot or spiritous internal or external. Be on the lookout for secondary hemorrhage or of the patient complaining of a "greater weight or fullness" of limb which is attended by pulsation. Gunshot wounds of the chest: For emphysema of the thorax perform a paracentesis when the air gets into the lung cavity and breathing becomes difficult; for external emphysema incise. . . . Burns are treated with linseed oil, cerate, wax, and spermaceti.

Such were the views and the advice of a patriotic surgeon to the younger men of his profession. It is true that there is nothing original in the Colonial's contribution. That privilege is reserved for a lucky few. Fortune smiles all too infrequently upon medicine and it is only a favored century that produces a Fallopius, a Harvey, or a Roentgen. Jones had the gift of collecting and analyzing the work of his contemporaries and was aptly able to express the thoughts of others. He was the first of a long line of distinguished American compilers. These men did no scintillating research. They made no attempt to fasten their names upon a medicine, a surgical instrument, or a fracture. But though their reputation was often transient and short-lived, they were of great influence during their time and age and were frequently of great service not only to their patients and pupils but to their country as well.

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# BOOK REVIEWS

## Tumors of the Female Pelvic Organs. By Joe Vincent Meigs, M.D., F.A.C.S. N. Y., Macmillan Co., 1934.

Dr. Meigs has written a valuable book. He begins with the accumulated pathological knowledge of the tumors of each organ, and then he correlates with these facts the clinical symptoms and signs produced in the patient and discusses the appropriate methods of treatment. Following this he has selected a small but carefully studied series of cases which have been followed up after treatment or operation. These were selected from the laboratories and wards of the Massachusetts General Hospital. By this method we are able to learn the results of treatment in each case—a splendid method. The book covers its field. It is well written and adequately illustrated. It is one of a series of surgical monographs of which Elliott C. Cutler, M.D., is editorial advisor. A foreword is written by Dr. Robert B. Greenough. This work is invaluable to the surgeon and gynecologist.

## Bronchoscopy, Esophagoscopy and Gastroscopy. A Manual of Peroral Endoscopy and Laryngeal Surgery. By Chevalier Jackson, M.D., SC.D., LL.D., F.A.C.S. and Chevalier L. Jackson, A.B., M.D., M.SC. (MED.), F.A.C.S. Ed. 3, reset. Phila., W. B. Saunders Co., 1934.

The third edition of Bronschoscopy, Esophagoscopy and Gastroscopy is an elaboration of the second edition which was so very well received.

There are an added number of illustrations and colored plates which bring out so many more of the masterful points in the old master himself. This volume emphasizes to a greater degree the value of bronchoscopy, not only in the extraction of foreign bodies, but for diagnosis and treatment of diseases of the lungs. The new feature: gastroscopy, is indeed worth mentioning.

This work has more than earned a place for itself in the library of not only the bronchoscopist but in that of the general practitioner whose perusal of this work will give him a better understanding, and so tend for greater cooperation between the family physician and the bronchoscopist.

## Entwicklung der Augenheilkunde im 18. und 19. Jahrhundert mit Besonderer Berücksichtigung der Schweiz. Nachlass Von Prof. Horner, Zürich. By Dr. Alfred Bader. Basel, Benno Schwabe & Co., 1933.

This work tells of the beginnings of the specialty of Ophthalmology in Switzerland, from the days when the surgery of the eye was largely in the hands of wandering quacks, like the Chevalier Taylor, on, throughout the eighteenth century, and well into the middle of the nineteenth. It is particularly a memorial of the development of the science, after Ophthalmology began to be treated with respect by medical educators and practitioners. It speaks of the struggles in Switzerland, in the fifties and sixties of the last century, for the emancipation of Ophthalmology from the domination of those general practitioners, who, without fitting themselves by an intense study of the eye, maintained that they had the right to deal with ophthalmological questions.

In the front ranks of that struggle stood Johann Friedrich Horner, of Zürich. The author offers this delightfully interesting little book to commemorate the centenary of Horner's birth, which occurred March 27, 1831. Horner, after receiving his degree in 1854, proceeded to Vienna for study in Arlt's clinic, later to Berlin, where for a time he was an assistant to von Graefe, and then on to Paris to work in the clinic of Desmarres. On returning to Zürich he entered into practice, undertaking whatever came to hand. In 1862, he was appointed to the Chair of Ophthalmology in the University, which he held until his death, from apoplexy, December 20, 1886.

Horner labored unceasingly to establish his chosen science into the position which Ophthalmology occupies in Switzerland today. He was a lucid and forceful teacher and drew to himself hosts of students from all over Europe and America. His strength lay in his insight as a diagnostician, and skill as an operator. He

was an untiring clinician with but little interest in laboratory routine. He was usually too exhausted at the end of his day's practice to compose himself for literary labor. Notwithstanding, he did contribute a number of papers, among which were those describing Herpes of the Cornea; and in 1869, the so-called "Horner's syndrome": enophthalmos, ptosis, contraction of the pupil, and unilateral sweating, expressive of cervical sympathetic nerve lesion.

The special feature of this memorial is a collection of one hundred and sixty letters addressed to Horner in Zürich, from many famous men in the ophthalmic world, among them: von Graefe, Billroth, Arlt, Krönlein, Donders, Helmholtz, Snellen, Duke Carl Theodor, of Bavaria, and Dufour. It is to be regretted that Horner's letters which had given rise to those that are here printed in full have not been given; apparently, all of Horner's have been lost. The letters show the thrill of enthusiasm which animated the spirit of the great observers, discoverers, and teachers of the middle of the last century, when modern Ophthalmology was born. The subjects discussed are of vital interest, relate to the progress of the science of Ophthalmology, and cover the period from 1855 to 1886. Many sidelights are exhibited, not the least being the display of the personalities of the writers. Some of the letters are quite lengthy; others only brief notes. In them we are reminded of von Graefe's venturesome surgical procedures and the revelations of the ophthalmoscopic studies of the fundus; Donders' pronouncements in the fields of accommodation and refraction; and Pasteur's and Lister's teachings relating to antisepsis.

Horner attracted all men to him by his character and personal charm. His ability as an ophthalmologist received recognition from a wide circle of scientists throughout Europe with whom he was in correspondence. All of the letters are most intimate and friendly and from them one learns that Horner was a lovable man, determined, yet kindly; a good correspondent.

Bader presents as an introduction to the letters an essay of eighty pages including the history of Swiss Ophthalmology. There are many portrait illustrations and facsimiles of letters, besides tables to show the lines of descent of the famous teachers and their equally distinguished pupils, and one, the transmission of practice in cataract operation, from Daviel to the beginning of this century. It is a beautifully made book of two hundred and thirty-one pages, with a copious index.

## Investigations of Postoperative Acidosis and Ketonuria. *Acta Chirurgica Scandinavica*, Vol. lxxiv, Suppl. xxix.* By Fredrik Roscher, Oslo, Kirstes Boktrykkeri, 1933.

This volume contains a rather lengthy discussion of the occurrence of ketonuria and acidosis after operation performed under inhalation narcosis with ether, chloroform and ethyl chloride. After inhalation anesthesia there was found a marked ketonuria usually lasting about twenty-four hours. Beginning with the narcosis there was a hyperglycemia of from 50 to 80 per cent. Operations under local anesthesia, with the exception of those for exophthalmic goiter, either leave the blood sugar unchanged or raised slightly. In operations on exophthalmic goiter, the usual hyperglycemia is increased after operation. The blood sugar rises a little after operation under spinal anesthesia.

Ketonuria is sometimes associated with a slight ketonemia. The ketosis with hyperglycemia is explained as being due to the mobilization of glycogen from the liver and possibly from other organs, while at the same time oxidation throughout the body is lessened. If renal function is not impaired, there is an increased secretion of nitrogen in the urine without nitrogen retention in the body. This increase is supposed to be due to a toxic endogenous decomposition of albumin produced by the narcosis. The phenomenon does not appear until the second day after operation and then the increased secretion of nitrogen may remain for from eight to ten days.

In children operated on, the ketonuria is usually more intense than in adults. The fact that this is commonly associated with hyperglycemia shows that it is not due to hunger.

Most patients do not need special treatment for the ketosis. A secondary hunger acidosis can be avoided by giving carbohydrates. In addition, the usual saline injections may be given.

* Abstracted by Samuel Amberg, M.D.

THE LIFE OF SIR ROBERT JONES. By Frederick Watson, M.D. Balt., William Wood & Co., 1934.

Every orthopedist will be interested in The Life of Sir Robert Jones, the most prominent orthopedist of modern times. All surgeons will find this book of exceeding interest. It is written in a charming style with a keen sense of proportion.

DIE MODERNE FINSENBEHANDLUNG. By Dr. Svend Lomholt. Berlin, Urban & Schwarzenberg, 1934.

This little monograph of 64 pages gives the latest development of the Finsen-Lomholt light treatment and brings up-to-date the older monographs on the subject. Originally printed in *Strablentberapie*, it has been found worthy of reprinting and will surely be of interest to all who use this method of treatment.

HANDBUCH DER GESAMTEN UNFALLHEILKUNDE, Vol. 4, No. 2, Pt. 2, pp. 9–18 and Pt. 3, pp. 19–28. By Dr. Fritz Konig & Dr. Georg Magnus. Stuttgart, Ferdinand Enke, 1934.

As the parts of the Handbuch der Gasamten Unfallheilkunde come along, they whet the appetite still further for the publication of the complete system which will be a splendid work of reference for all interested in industrial surgery.

## BOOKS RECEIVED

All books received by THE AMERICAN JOURNAL OF SURGERY are listed in this column as soon as possible after their receipt and this must be considered as adequate acknowledgment. Books that the Editor considers of special interest to our readers will be reviewed in a later issue.

AMEBIASIS AND AMEBIC DYSENTERY. By Charles F. Craig, M.D. Springfield, Ill., Charles C. Thomas, 1934.

ANATOMY OF SURGICAL APPROACHES (THE). By L. C. Kellogg, M.D. Balt., Williams & Wilkins Co., 1934.

APPLIED ANATOMY. By Gwilym G. Davis, M.D. Ed. 9, Phila., J. B. Lippincott Co., 1934.

ARQUIVO DE PATOLOGIA. By F. Gentil, M.D. and M. Athias, M.D. Vol. 6, No. 1, Palhava-Lisboa, April, 1934.

ATTORNEY'S TEXTBOOK OF MEDICINE. By Roscoe N. Gray. Albany, Matthew Bender & Co., 1934.

AUTONOMIC NERVOUS SYSTEM (THE). By Albert Kuntz, M.D. Ed. 2, Phila., Lea & Febiger, 1934.

CATARACT—ITS ETIOLOGY AND TREATMENT. By Clyde A. Clapp, M.D. Phila., Lea & Febiger, 1934.

CHIRURGIE DER PANCRÉAS. By P. Brocq, M.D. and G. Miginiac, M.D. Paris, Masson et Cie, 1934.

CONCEPTION PERIOD OF WOMEN. By K. Ogino, M.D. Harrisburg, Pa., Med. Arts Pub. Co., 1934.

GYNECOLOGY. By Brooke M. Anspach, M.D. Ed. 5, Phila., J. B. Lippincott Co., 1934.

INTERNATIONAL CLINICS. Ed. by Louis Hamman, M.D. S. 44, Vol. 3, Phila., J. B. Lippincott Co., 1934.

MATERNAL MORTALITY IN PHILADELPHIA, 1931–1933. Philadelphia County Medical Society. Phila., 1934.

MINOR SURGERY FOR THE GENERAL PRACTITIONER. By William T. Gibb, M.D. N. Y., Paul B. Hoeber, Inc., 1934.

OPERATIONSTAKTIK BEI ERKRANKUNGEN DER GALLENWEGE. By W. M. Stern, M.D. and R. Fourche, M.D. Berlin, Urban und Schwarzenberg, 1934.

OSTEOMYELITIS. By Abraham O. Wilensky, M.D. N. Y. Macmillan Co., 1934.

PHYSICAL DIAGNOSIS. By Richard C. Cabot, M.D. Ed. 11, Balt., Williams & Wilkins Co., 1934.

PRACTICAL TALKS ON HEART DISEASE. By George L. Carlisle, M.D. Springfield, Charles C. Thomas, 1934.

RECENT ADVANCES IN PATHOLOGY. By Geoffrey Hadfield, M.D. and Lawrence P. Garrod, M.D. Ed. 2, Phila., P. Blakiston's Sons & Co., 1934.

ROCKEFELLER FOUNDATION ANNUAL REPORT, 1933. N. Y., Rockefeller Found., 1933.

RÖNTGENDIAGNOSTIK DER KNOCKEN- UND GELENKKRANKHEITEN. By Robert Kienböck, M.D. Berlin, Urban und Schwarzenberg, 1934.

SCIENCE AND PRACTICE OF SURGERY (THE). By W. H. C. Romanis, M.D. and Philip H. Mitchiner, M.D. Ed. 5, Phila., Lea and Febiger, 1934, 2 vols.

SPINAL ANESTESIA—TECHNIC AND CLINICAL APPLICATION. By George Rudolph Vehrs, M.D. St. Louis, C. V. Mosby Co., 1934.

SYNOPSIS OF GENITOURINARY DISEASES. By Austin I. Dodson, M.D. St. Louis, C. V. Mosby Co., 1934.

TEXTBOOK OF GYNECOLOGY (A). By Arthur Hale Curtis, M.D. Phila., W. B. Saunders Co., 1934.

TEXT-BOOK OF PATHOLOGY, (A). By Williams Boyd, M.D. Ed. 2, Phila., Lea & Febiger, 1934.

TREATMENT OF INJURIES OF THE HEAD AND SPINE. By Jewett V. Reed, M.D. Indianapolis, C. E. Pauley & Co., 1934.

TUBERCULOSIS OF THE LYMPHATIC SYSTEM. By Richard H. Miller, M.D. N. Y., Macmillan Co., 1934.

UNFALL UND HIRNGESCHWULST. By Otto Marburg, M.D. Vienna, Julius Springer, 1934.

VIE ET RAJEUNISSEMENT. By Francesco Cavazzi, M.D. Paris, Gaton Doin et Cie, 1934.

VISCERITI E PERIVISCERITI. By Francisco Zagarese, M.D. Bologna, S. A. Nicola Zanichelli, 1934.

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